

Intra-Cellular Therapies, Inc.  
Form 10-K  
February 25, 2016  
Table of Contents

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
**Washington, D.C. 20549**

**FORM 10-K**

(Mark One)

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2015**

**OR**

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the transition period from \_\_\_\_\_ to \_\_\_\_\_**

**Commission file number: 001-36274**

**Intra-Cellular Therapies, Inc.**

**(Exact name of registrant as specified in its charter)**

**Delaware**  
**(State or other jurisdiction of**  
**incorporation or organization)**

**36-4742850**  
**(I.R.S. Employer**  
**Identification No.)**

**430 East 29th Street**  
**New York, New York 10016**

**(Address of principal executive offices) (Zip Code)**

**Registrant's telephone number, including area code (212) 923-3344**

**Securities registered pursuant to Section 12(b) of the Exchange Act:**

<b>Title of each class</b>	<b>Name of each exchange on which registered</b>
<b>Common Stock, \$0.0001 Par Value Per Share</b>	<b>The NASDAQ Global Select Market</b>
<b>Securities registered pursuant to Section 12(g) of the Exchange Act: None</b>	

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Edgar Filing: Intra-Cellular Therapies, Inc. - Form 10-K

Large accelerated filer  Accelerated filer   
Non-accelerated filer  [Do not check if a smaller reporting company] Smaller reporting company   
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the registrant's most recently completed second fiscal quarter was \$750.7 million.

As of February 25, 2016, the registrant had 43,212,709 shares of common stock outstanding.

Table of Contents

## TABLE OF CONTENTS

	<b>Page</b>
<b><u>PART I</u></b>	4
Item 1. <u>Business</u>	4
Item 1A. <u>Risk Factors</u>	29
Item 1B. <u>Unresolved Staff Comments</u>	52
Item 2. <u>Properties</u>	52
Item 3. <u>Legal Proceedings</u>	52
Item 4. <u>Mine Safety Disclosures</u>	52
<b><u>PART II</u></b>	53
Item 5. <u>Market For Registrant's Common Equity, Related Stockholder Matters And Issuer Purchases Of Equity Securities</u>	53
Item 6. <u>Selected Financial Data</u>	55
Item 7. <u>Management's Discussion And Analysis Of Financial Condition And Results Of Operations</u>	56
Item 7A. <u>Quantitative And Qualitative Disclosures About Market Risk</u>	71
Item 8. <u>Financial Statements And Supplementary Data</u>	71
Item 9. <u>Changes In And Disagreements With Accountants On Accounting And Financial Disclosure</u>	71
Item 9A. <u>Controls And Procedures</u>	71
Item 9B. <u>Other Information</u>	73
<b><u>PART III</u></b>	74
Item 10. <u>Directors, Executive Officers And Corporate Governance</u>	74
Item 11. <u>Executive Compensation</u>	74
Item 12. <u>Security Ownership Of Certain Beneficial Owners And Management And Related Stockholder Matters</u>	74
Item 13. <u>Certain Relationships And Related Transactions, And Director Independence</u>	74
Item 14. <u>Principal Accounting Fees And Services</u>	74
<b><u>PART IV</u></b>	75
Item 15. <u>Exhibits, Financial Statement Schedules</u>	75
<u>Signatures</u>	79

**Table of Contents**

**DOCUMENTS INCORPORATED BY REFERENCE**

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated by reference from the Registrant's Proxy Statement for the 2016 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission.

---

**Table of Contents****PART I**

*All brand names or trademarks appearing in this report are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this report is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners. Unless the context requires otherwise, references in this report to the Company, we, us, and our refer to Intra-Cellular Therapies, Inc. and its wholly-owned subsidiary, ITI, Inc.*

**Item 1. BUSINESS****Overview**

We are a biopharmaceutical company focused on the discovery and clinical development of innovative, small molecule drugs that address underserved medical needs in neuropsychiatric and neurological disorders by targeting intracellular signaling mechanisms within the central nervous system, or CNS. ITI-007 is our lead drug development candidate with mechanisms of action that, we believe, may represent an effective treatment across multiple therapeutic indications. In our pre-clinical and clinical trials to date, ITI-007 combines potent serotonin 5-HT<sub>2A</sub> receptor antagonism, dopamine receptor phosphoprotein modulation, or DPPM, glutamatergic modulation, and serotonin reuptake inhibition into a single drug candidate for the treatment of acute and residual schizophrenia and the treatment of bipolar disorder, including bipolar depression. At dopamine D<sub>2</sub> receptors, ITI-007 has been demonstrated to have dual properties and to act as both a pre-synaptic partial agonist and a post-synaptic antagonist. ITI-007 has also been demonstrated to have affinity for dopamine D<sub>1</sub> receptors and indirectly stimulate phosphorylation of glutamatergic NMDA GluN<sub>2B</sub> receptors in a mesolimbic specific manner. We believe that this regional selectivity in brain areas thought to mediate the efficacy of antipsychotic drugs, together with serotonergic, glutamatergic, and dopaminergic interactions, may result in efficacy for a broad array of symptoms associated with schizophrenia and bipolar disorder with improved psychosocial function. The serotonin reuptake inhibition potentially allows for antidepressant activity in the treatment of schizoaffective disorder, other disorders with co-morbid depression, and/or as a stand-alone treatment for major depressive disorder. We believe ITI-007 may also be useful for the treatment of other psychiatric and neurodegenerative disorders, particularly behavioral disturbances associated with dementia, autism, and other CNS diseases. ITI-007 is in Phase 3 clinical development as a novel treatment for schizophrenia and bipolar depression.

*ITI-007 for the Treatment of Schizophrenia*

In September 2015, we announced top-line clinical results from our first Phase 3 clinical trial of ITI-007 for the treatment of patients with schizophrenia. This randomized, double-blind, placebo-controlled Phase 3 clinical trial was conducted at 12 sites in the United States with 450 patients randomized (1:1:1) to receive either 60 mg of ITI-007, 40 mg of ITI-007 or placebo once daily in the morning for 28 days. The pre-specified primary efficacy measure was change from baseline versus placebo at study endpoint (4 weeks) on the centrally rated Positive and Negative Syndrome Scale, or PANSS, total score. In this trial, the once-daily dose of 60 mg of ITI-007 met the primary endpoint and demonstrated antipsychotic efficacy with statistically significant superiority over placebo at week 4 (study endpoint) with additional improvements observed in social function. Moreover, the 60 mg dose of ITI-007 showed significant antipsychotic efficacy as early as week 1, which was maintained at every time point throughout the entire study. ITI-007 showed a dose-related improvement in symptoms of schizophrenia with the 40 mg dose approximating the trajectory of improvement seen with the 60 mg dose, but the effect with 40 mg did not reach statistical significance on the primary endpoint. In addition, the 60 mg dose of ITI-007 met the key secondary endpoint of statistically significant improvement on the Clinical Global Impression Scale for Severity of Illness, or

CGI-S. The 40 mg dose of ITI-007 also demonstrated a statistically significant improvement versus placebo on the CGI-S, though not formally tested against placebo as a key secondary endpoint since it did not separate on the primary endpoint. Consistent with previous studies, ITI-007 had a favorable safety and tolerability profile as evidenced by motoric, metabolic, and cardiovascular characteristics similar to placebo, and no clinically significant changes in akathisia, extrapyramidal symptoms, prolactin, body weight, glucose, insulin, or lipids.

---

**Table of Contents**

In September 2015, we also announced top-line data from an open-label positron emission tomography, or PET, study of ITI-007 examining brain occupancy of striatal D<sub>2</sub> receptors. This study was conducted in patients diagnosed with schizophrenia who were otherwise healthy and stable with respect to their psychosis. After washout from their previous antipsychotic medication for at least two weeks, PET was used to determine target occupancy in brain regions at baseline (drug-free) and again after two weeks of once daily ITI-007 oral administration. In this trial, the 60 mg dose of ITI-007 was associated with a mean of approximately 40% striatal dopamine D<sub>2</sub> receptor occupancy. As predicted by preclinical and earlier clinical data, ITI-007 demonstrated antipsychotic effect at relatively low striatal D<sub>2</sub> receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D<sub>2</sub> receptors. We believe this mechanism likely contributes to the favorable safety profile of ITI-007, with reduced risk for hyperprolactinemia, akathisia, extrapyramidal symptoms, and other motoric side effects.

The top-line results from our first Phase 3 clinical trial of ITI-007 confirm the earlier Phase 2 results that we announced in December 2013, in which ITI-007 exhibited antipsychotic efficacy in a randomized, double-blind, placebo and active controlled clinical trial in patients with an acutely exacerbated episode of schizophrenia. In this Phase 2 trial, 335 patients were randomized to receive one of four treatments: 60 mg of ITI-007, 120 mg of ITI-007, 4 mg of risperidone (active control) or placebo in a 1:1:1:1 ratio, orally once daily for 28 days. The primary endpoint for this clinical trial was change from baseline to Day 28 on the PANSS total score. In this study, ITI-007 met the trial's pre-specified primary endpoint, improving symptoms associated with schizophrenia as measured by a statistically significant and clinically meaningful decrease in the PANSS total score. The trial also met key secondary outcome measures related to efficacy on PANSS subscales and safety. We are also conducting a second Phase 3 clinical trial in schizophrenia that we initiated in the second quarter of 2015, with over 600 patients planned to be enrolled in the trial. In this trial, we are randomizing patients to two doses of ITI-007 (60 mg or 20 mg), risperidone (active control) or placebo over a 6-week treatment duration, and the primary outcome measure is change from baseline to Day 42 on the PANSS total score. We expect patient enrollment will be completed in the second quarter of 2016. Subject to timely enrollment, we anticipate top-line results from the second Phase 3 clinical trial will be available in mid-2016.

In addition to our two Phase 3 clinical trials, we will need to complete other clinical and non-clinical trials and manufacturing and pre-commercialization activities necessary to support the submission of a planned New Drug Application, or NDA, for ITI-007 in schizophrenia, which we currently expect could occur in the first half of 2017.

*ITI-007 for the Treatment of Depressive Episodes Associated with Bipolar Disorder (Bipolar Depression)*

Our bipolar depression program consists of two Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials: one to evaluate ITI-007 as a monotherapy and the other to evaluate ITI-007 as an adjunctive therapy with lithium or valproate. In each trial, approximately 550 patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode will be randomized to receive one of three treatments: 60 mg ITI-007, 40 mg ITI-007, or placebo in a 1:1:1 ratio orally once daily for 6 weeks. In the ITI-007-401 trial, patients will receive ITI-007 or placebo as a monotherapy. In the ITI-007-402 trial, patients will receive ITI-007 or placebo adjunctive to their existing mood stabilizer lithium or valproate. We initiated our bipolar depression program in the third quarter of 2015.

The primary endpoint for both clinical trials is change from baseline at Day 42 on the Montgomery-Åsberg Depression Rating Scale, or MADRS, total score versus placebo. The MADRS is a well-validated 10-item checklist that measures the ability of a drug to reduce overall severity of depressive symptoms. Individual items are rated by an expert clinician on a scale of 0 to 6 in which a score of 6 represents the most depressed evaluation for each item assessed. The total score ranges from 0 to 60. Secondary endpoints include measures of social function and quality of



life that may illustrate the differentiated clinical profile of ITI-007. Safety and tolerability are also assessed in both clinical trials.

---

**Table of Contents***Other Indications for ITI-007*

In the fourth quarter of 2014, we announced the top-line data from ITI-007-200, a Phase 1/2 clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of ITI-007 in healthy geriatric subjects and in patients with dementia, including Alzheimer's disease. The completion of this study marks an important milestone in our strategy to develop low doses of ITI-007 for the treatment of behavioral disturbances associated with dementia and related disorders. The ITI-007-200 trial results to date indicate that ITI-007 is safe and well-tolerated across a range of low doses, has linear- and dose-related pharmacokinetics and improves cognition in the elderly. The most frequent adverse event was mild sedation at the higher doses. We believe these results further position ITI-007 as a development candidate for the treatment of behavioral disturbances in patients with dementia and other neuropsychiatric and neurological conditions. We plan to initiate late phase clinical programs evaluating ITI-007 in patients with behavioral disturbances associated with dementia and related disorders, including Alzheimer's disease, in the first half of 2016.

We are also pursuing clinical development of ITI-007 for the treatment of additional CNS diseases and disorders. At the lowest doses, ITI-007 has been demonstrated to act primarily as a potent 5-HT<sub>2A</sub> serotonin receptor antagonist. As the dose is increased, additional benefits are derived from the engagement of additional drug targets, including modest dopamine receptor modulation and modest inhibition of serotonin transporters. We believe that combined interactions at these receptors may provide additional benefits above and beyond selective 5-HT<sub>2A</sub> antagonism for treating agitation, aggression and sleep disturbances in diseases that include dementia, Alzheimer's disease, Huntington's disease and autism spectrum disorders, while avoiding many of the side effects associated with more robust dopamine receptor antagonism. As the dose of ITI-007 is further increased, leading to moderate dopamine receptor modulation, inhibition of serotonin transporters, and indirect glutamate modulation, these actions complement the complete blockade of 5-HT<sub>2A</sub> serotonin receptors. At a dose of 60 mg, ITI-007 has been shown effective in treating the symptoms associated with schizophrenia, and we believe this higher dose range will be useful for the treatment of bipolar disorder, depressive disorders and other neuropsychiatric diseases.

Given the potential utility for ITI-007 and follow-on compounds to treat these additional indications, we may investigate, either on our own or with a partner, agitation, aggression and sleep disturbances in additional diseases that include autism spectrum disorders; depressive disorder; intermittent explosive disorder; non-motor symptoms and motor complications associated with Parkinson's disease; and post-traumatic stress disorder. We hold exclusive, worldwide commercialization rights to ITI-007 and a family of compounds from Bristol-Myers Squibb Company pursuant to an exclusive license.

*Other Product Candidates*

We have a second major program called ITI-002 that has yielded a portfolio of compounds that selectively inhibits the enzyme phosphodiesterase type 1, or PDE1. We believe PDE1 helps regulate brain activity related to cognition, memory processes and movement/coordination. On February 25, 2011, we (through our wholly owned operating subsidiary, ITI) and Takeda Pharmaceutical Company Limited, or Takeda, entered into a license and collaboration agreement, or the Takeda License Agreement, under which we agreed to collaborate to research, develop and commercialize our proprietary compound ITI-214 and other selected compounds that selectively inhibit PDE1 for use in the prevention and treatment of human diseases. On October 31, 2014, we entered into an agreement with Takeda terminating the Takeda License Agreement, or the Termination Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. On September 15, 2015, Takeda completed the transfer of the Investigational New Drug application, or IND, for ITI-214 to us. ITI-214 is the first compound in its class to successfully advance into Phase 1 clinical trials. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's

disease, cognition in Alzheimer's disease, cognition in schizophrenia and in other non-CNS indications. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

## **Table of Contents**

Our pipeline also includes pre-clinical programs that are focused on advancing drugs for the treatment of schizophrenia, Parkinson's disease, Alzheimer's disease and other neuropsychiatric and neurodegenerative disorders. We are also investigating the development of treatments for disease modification of neurodegenerative disorders and non-CNS diseases.

We have assembled a management team with significant industry experience to lead the discovery and development of our product candidates. We complement our management team with a group of scientific and clinical advisors that includes recognized experts in the fields of schizophrenia and other CNS disorders, including Nobel laureate, Dr. Paul Greengard, one of our co-founders.

We were originally incorporated in the State of Delaware in August 2012 under the name Oneida Resources Corp. Prior to a reverse merger that occurred on August 29, 2013, or the Merger, Oneida Resources Corp. was a shell company registered under the Securities Exchange Act of 1934, or the Exchange Act, with no specific business plan or purpose until it began operating the business of ITI, Inc., or ITI, through the Merger transaction on August 29, 2013. ITI was incorporated in Delaware in May 2001 to focus primarily on the development of novel drugs for the treatment of neuropsychiatric and neurologic diseases and other disorders of the CNS. Effective upon the Merger, a wholly-owned subsidiary of the Company merged with and into ITI, and ITI continues as the operating subsidiary of the Company. As used herein, the words the Company, we, us, and our refer to the current Delaware corporation operating the business of ITI as a wholly-owned subsidiary, which business continues as the business of the Company.

Our corporate headquarters and laboratory are located at 430 East 29th Street, New York, New York 10016, and our telephone number is (646) 440-9333. We also have an office in Towson, Maryland. We maintain a website at [www.intracellulartherapies.com](http://www.intracellulartherapies.com), to which we regularly post copies of our press releases as well as additional information about us. Our filings with the SEC will be available free of charge through the Investor Relations section of our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website does not constitute a part of this report or our other filings with the SEC.

## **Our Strategy**

Our goal is to discover and develop novel small molecule therapeutics for the treatment of CNS diseases in order to improve the lives of people suffering from such illnesses. Using our key understanding of intracellular signaling, we seek to accomplish our goal, using our in-house expert drug discovery and clinical development teams, in two ways:

we seek to have the capability to develop first-in-class medications with novel mechanisms that have the potential to treat CNS diseases for which there are no previously marketed drugs; and

we seek to develop drugs that either can differentiate themselves in competitive markets by addressing aspects of CNS disease which are not treated by currently marketed drugs or can be effective with fewer side effects.

The key elements of our strategy are to:

complete the development of ITI-007 for its lead indication, treatment of schizophrenia, and for additional neuropsychiatric indications, such as bipolar disorder and residual symptoms in schizophrenia;

expand the commercial potential of ITI-007 by investigating its usefulness in neurological areas, such as behavioral disturbances in dementia, including Alzheimer's disease and autism spectrum disorder, and in additional neuropsychiatric indications, such as sleep disorders associated with neuropsychiatric and neurological disorders and major depressive disorder;

## **Table of Contents**

continue to develop PDE inhibitor compounds, such as ITI-214, for the treatment of CNS and other disorders; and

advance earlier stage product candidates in our pipeline.

## **Our Drug Discovery Platform and Capabilities**

Based on the pioneering efforts of our co-founder and Nobel laureate, Dr. Paul Greengard, we have developed a detailed understanding of intracellular signaling pathways and intracellular targets. We have used that knowledge to develop several state of the art technology platforms, including one called CNSProfile™. This technology monitors the phosphoprotein changes elicited by major psychotropic drug classes and subclasses, and generates a unique molecular signature for drug compounds. By monitoring how the levels of these phosphoproteins change *in vivo*, we identify intracellular signaling pathways through which several major drug classes operate. Along with what we believe to be state of the art drug discovery efforts, we have used, and may continue to use, this information as a tool to validate our selection of preclinical candidate molecules.

During the years ended December 31, 2015 and 2014, we incurred \$87.7 million and \$21.2 million in research and development expenses, respectively.

Given the nature of our research and development and business activities, we do not expect that compliance with federal, state and local environmental laws will result in material costs or have a significant negative effect on our operations.

## **Disease and Market Overview**

Our programs for small molecule therapeutics are designed to address various CNS diseases that we believe are underserved or unmet by currently available therapies and that represent large potential commercial market opportunities for us. Background information on the CNS diseases and related commercial markets that may be addressed by our programs is set forth below.

### ***Schizophrenia***

Schizophrenia is a disabling and chronic mental illness that is characterized by multiple symptoms during an acute phase of the disorder that can include so-called positive symptoms, such as hearing voices, grandiose beliefs and suspiciousness or paranoia. These symptoms can be accompanied by additional, harder to treat symptoms, such as social withdrawal, blunted emotional response and speech deficits, collectively referred to as negative symptoms, difficulty concentrating and disorganized thoughts, or cognitive impairment, depression and insomnia. Such residual symptoms often persist even after the acute positive symptoms subside, and contribute substantially to the social and employment disability associated with schizophrenia. Current antipsychotic medications provide some relief for the symptoms associated with the acute phase of the disorder, but they do not effectively treat the residual phase symptoms associated with chronic schizophrenia. Currently available medications used to treat acute schizophrenia are limited in their use due to side effects that can include movement disorders, weight gain, metabolic disturbances, and cardiovascular disorders. Indeed, the side effects associated with current antipsychotic medications often make some of the residual phase symptoms, such as negative symptoms and social function, worse. There is an unmet medical need for new therapies that have improved side effect and efficacy profiles.

According to the National Institute of Mental Health, over 1% of the world's population suffers from schizophrenia, and more than 2.5 million Americans suffer from the illness in any given year. Worldwide sales of antipsychotic drugs

exceeded \$14 billion in 2014. These drugs have been increasingly used by physicians to address a range of disorders in addition to schizophrenia, including bipolar disorder and a variety of psychoses and related conditions in elderly patients. Despite their commercial success, current antipsychotic drugs have substantial limitations, including inadequate efficacy and severe side effects.

## **Table of Contents**

The first-generation, or typical, antipsychotics that were introduced in the late-1950s block dopamine receptors. While typical antipsychotics are effective against positive symptoms of schizophrenia in many patients, these drugs often induce disabling motor disturbances, and they fail to address or worsen most of the negative symptoms and cognitive disturbances associated with schizophrenia.

Most schizophrenia patients in the United States are treated today with second-generation, or atypical, antipsychotics, which induce fewer motor disturbances than typical antipsychotics, but still fail to address most of the negative symptoms of schizophrenia and other symptoms associated with social function impairment. Many patients with schizophrenia have deficits in social function. Social function is the ability to recognize, understand, process and use external cues to solve problems, maintain work performance, and conduct interpersonal relationships. Deficits in social function often remain after positive symptoms, such as hallucinations and delusions, have resolved in these patients. In addition, currently prescribed treatments do not effectively address or may exacerbate cognitive disturbances associated with schizophrenia. It is believed that the efficacy of atypical antipsychotics is due to their interactions with dopamine and 5-HT<sub>2A</sub> receptors. The side effects induced by the atypical agents may include weight gain, non-insulin dependent (type II) diabetes, cardiovascular side effects, sleep disturbances, and motor disturbances. We believe that these side effects generally arise either from non-essential receptor interactions or from excessive dopamine blockade.

The limitations of currently available antipsychotics result in poor patient compliance. A landmark study funded by the National Institute of Mental Health, the Clinical Antipsychotic Trials of Intervention Effectiveness, also referred to as CATIE, which was published in The New England Journal of Medicine in September 2005, found that 74% of patients taking typical or atypical antipsychotics discontinued treatment within 18 months because of side effects or lack of efficacy. We believe there is a large underserved medical need for new therapies that have improved side effect and efficacy profiles.

## ***Bipolar Disorder***

Bipolar disorder, sometimes referred to as manic-depressive illness, is characterized by extreme shifts in mood. Individuals with bipolar disorder may experience intense feelings of over-excitement, irritability, and impulsivity with grandiose beliefs and racing thoughts, referred to as a manic episode. Symptoms of depression may include feeling tired, hopeless and sad, with difficulty concentrating and thoughts of suicide. Some people experience both types of symptoms in the same mixed episode. Severe symptoms of bipolar disorder can be associated with hallucinations or delusions, otherwise referred to as psychosis.

Bipolar disorder affects approximately 5.7 million adults in the United States in any given year, or about 2.6 percent of the adult U.S. population. In 2012, therapeutics used to treat bipolar disorder had global sales of approximately \$6 billion.

Bipolar disorder is often treated with antipsychotic medications alone or in combination with mood stabilizers. The side effects and safety risks associated with antipsychotic drugs in patients with bipolar disorder are similar to those experienced by patients with schizophrenia. Moreover, a large national research program conducted from 1998 to 2005 called the Systematic Treatment Enhancement Program for Bipolar Disorder, or STEP-BD, followed 4,360 patients with bipolar disorder long term and showed that about half of patients who were treated for bipolar disorder still experienced lingering and recurrent symptoms, indicating a clear need for improved treatments.

## ***Behavioral Disturbances in Dementia, Including Alzheimer's Disease***



It has been estimated that 44.4 million people worldwide were living with dementia in 2013, including over 5.2 million patients with Alzheimer's disease in the United States. This number is expected to increase to 75.6 million by 2030 and to increase to 135.5 million by 2050. While the diagnostic criteria for Alzheimer's disease and other dementias mostly focus on the related cognitive deficits, it is often the behavioral and psychiatric symptoms that are most troublesome for caregivers and lead to poor quality of life for patients.

## **Table of Contents**

Several behavioral symptoms are quite prevalent in patients with dementia, including patients with Alzheimer's disease. In view of the potential multiple effects of ITI-007 on aggression, agitation, sleep disorders and depression, and its safety profile to date, we believe that ITI-007 may provide a novel therapy for treating the behavioral disturbances accompanying dementia, including Alzheimer's disease.

The FDA has not approved any drug to treat the behavioral symptoms of dementia, including Alzheimer's disease. As symptoms progress and become more severe, physicians often resort to off-label use of antipsychotic medications in these patients. Current antipsychotic drugs are associated with a number of side effects, which can be problematic for elderly patients with dementia. In addition, antipsychotic drugs may exacerbate the cognitive disturbances associated with dementia. We believe there is a large unmet medical need for a safe and effective therapy to treat the behavioral symptoms in patients with dementia, including Alzheimer's disease.

### ***Alzheimer's Disease***

Alzheimer's disease is a progressive neurodegenerative disorder that slowly destroys memory and thinking skills, and eventually even the ability to carry out simple tasks. Its symptoms include cognitive dysfunction, memory abnormalities, progressive impairment in activities of daily living, and a host of behavioral and neuropsychiatric symptoms. Alzheimer's disease primarily affects older people and, in most cases, symptoms first appear after age 60. Alzheimer's disease gets worse over time and is fatal.

The market for Alzheimer's disease therapeutics is categorized into two segments: acetylcholinesterase inhibitors and NMDA receptor antagonists, which include Aricept<sup>®</sup>, Namenda<sup>®</sup>, Exelon<sup>®</sup> and Ebixa<sup>®</sup>. These two segments had total sales of \$4.9 billion in 2013.

According to the Alzheimer's Association, 5.2 million people in the United States are living with Alzheimer's disease, and it is currently the fifth leading cause of death for people age 65 and older. It has been estimated that 44.4 million people worldwide were living with dementia in 2013. This number is expected to increase to 75.6 million by 2030 and to increase to 135.5 million by 2050. While the diagnostic criteria for Alzheimer's disease mostly focus on the related cognitive deficits, it is often the behavioral and psychiatric symptoms that are most troublesome for caregivers and lead to poor quality of life for patients. These symptoms include agitation, aggressive behaviors, depression, sleep disorders, and psychosis. Studies have suggested that approximately 60% of patients with Alzheimer's disease experience agitation/aggression, up to 87% of patients experience depression, approximately 60% of patients experience sleep disturbances, particularly as an increased likelihood of day-night reversal, and approximately 20% to 51% of Alzheimer's disease patients may develop psychosis at some point in the disease process, commonly consisting of hallucinations and delusions. The diagnosis of Alzheimer's disease psychosis is associated with more rapid cognitive and functional decline and institutionalization. Sleep disturbances increase the likelihood of day-night reversion, increased agitation and increased caregiver stress that strongly influences decisions for nursing home placement.

The FDA has not approved any drug to treat the behavioral symptoms of Alzheimer's disease. As symptoms progress and become more severe, physicians often resort to off-label use of antipsychotic medications in these patients. Current antipsychotic drugs are associated with a number of side effects, which can be problematic for elderly patients with Alzheimer's disease. In addition, antipsychotic drugs may exacerbate the cognitive disturbances associated with Alzheimer's disease. Current antipsychotic drugs also have a boxed warning for use in elderly patients with dementia-related psychosis due to increased mortality and morbidity. There is a large unmet medical need for a safe and effective therapy to treat the behavioral symptoms in patients with Alzheimer's disease.

### ***Parkinson's Disease***

Parkinson's disease is a chronic and progressive neurodegenerative disorder that involves malfunction and death of neurons in a region of the brain that controls movement. This neurodegeneration creates a shortage of an important brain signaling chemical, or neurotransmitter, known as dopamine, thereby rendering patients unable

## **Table of Contents**

to direct or control their movements in a normal manner. Parkinson's disease is characterized by well-known motor symptoms, including tremors, limb stiffness, slowness of movements, and difficulties with posture and balance, as well as by non-motor symptoms, which include sleep disturbances, mood disorders, cognitive impairment and psychosis. Parkinson's disease progresses slowly in most people and the severity of symptoms tends to worsen over time.

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. According to the National Parkinson Foundation, about 1 million people in the United States and from approximately 4 to 6 million people worldwide suffer from this disease. Parkinson's disease is more common in people over 60 years of age, and the prevalence of this disease is expected to increase significantly as the average age of the population increases. Parkinson's disease patients are commonly treated with dopamine replacement therapies, such as levodopa, commonly referred to as L-DOPA, which is metabolized to dopamine, and dopamine agonists, which are molecules that mimic the action of dopamine. Sales of therapeutics such as L-DOPA and dopamine agonists used to treat the motor symptoms of the disease reached \$2.3 billion in 2013.

Non-motor symptoms can be particularly distressing and even more troublesome to patients with Parkinson's disease than the primary motor disturbances. Non-motor symptoms substantially contribute to the burden of Parkinson's disease and deeply affect the quality of life of patients and their caregivers. Non-motor symptoms of Parkinson's disease are associated with increased caregiver stress and burden, nursing home placement, and increased morbidity and mortality.

Treatment of non-motor symptoms associated with Parkinson's disease poses a challenge to physicians. Current dopamine replacement drugs used to treat the motor symptoms of Parkinson's disease do not help, and sometimes worsen, the non-motor symptoms. No drugs are currently approved by the FDA for treating the broad non-motor symptoms associated with Parkinson's disease, and this remains a large unmet medical need.

## ***Depression***

Major depressive disorder, or MDD, is a brain disorder that can be associated with symptoms of sadness, hopelessness, helplessness, feelings of guilt, irritability, loss of interest in formerly pleasurable activities, cognitive impairment, disturbed sleep patterns, and suicide ideation or behavior. Different people may experience different symptoms, but everyone with major depression experiences symptoms that are severe enough to interfere with everyday functioning, such as the ability to concentrate at work or school, social interactions, eating and sleeping. Sometimes the depressive episode can be so severe it is accompanied by psychosis (hallucinations and delusions). According to the National Institute of Mental Health, approximately 3% of teenagers and approximately 7% of adults experience MDD each year. Worldwide sales of antidepressant drugs reached \$9.3 billion in 2013. The antidepressant market is primarily composed of selective serotonin reuptake inhibitors such as Lexapro® (marketed by Forest Laboratories and Lundbeck) and selective norepinephrine reuptake inhibitors, or SNRIs, such as Cymbalta® (marketed by Eli Lilly). Antipsychotics such as Seroquel® (marketed by Astrazeneca) and Abilify® (marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical) are also used as adjunctive treatments with antidepressant treatment. The National Institute of Mental Health-funded Sequenced Treatment Alternatives to Relieve Depression, or STAR\*D, study showed that only one-third of treated patients experience complete remission of depressive symptoms. Nearly two-thirds of patients were considered treatment-resistant.

## **Table of Contents**

### **Our Clinical Programs**

Our pipeline includes two product candidates in clinical development and two product candidates in advanced pre-clinical testing. We believe that our product candidates offer innovative therapeutic approaches and may provide significant advantages relative to current therapies. The following table summarizes our product candidates and programs:

### **OUR THERAPEUTIC PIPELINE**

#### ***ITI-007 Program***

Our lead product candidate, ITI-007, possesses mechanisms of action that we believe may represent an effective treatment across multiple therapeutic indications. ITI-007 is in Phase 3 clinical trials for the treatment of schizophrenia. In our pre-clinical and clinical trials to date, we have demonstrated that ITI-007 combines potent serotonin 5-HT<sub>2A</sub> receptor antagonism, dopamine receptor phosphoprotein modulation, or DPPM, glutamatergic modulation and serotonin reuptake inhibition into a single drug candidate for the treatment of acute and residual schizophrenia. At dopamine D<sub>2</sub> receptors, ITI-007 has been demonstrated to have dual properties and to act as both a pre-synaptic partial agonist and a post-synaptic antagonist. ITI-007 has also been demonstrated to have affinity for dopamine D<sub>1</sub> receptors and indirectly stimulate phosphorylation of glutamatergic NMDA NR<sub>2B</sub>, or GluN<sub>2B</sub>, receptors in a mesolimbic specific manner. We believe that this regional selectivity in brain areas thought to mediate the efficacy of antipsychotic drugs, together with serotonergic, glutamatergic, and dopaminergic interactions, may result in antipsychotic efficacy for positive, negative, affective and cognitive symptoms associated with schizophrenia. The serotonin reuptake inhibition could allow for antidepressant activity for the treatment of schizoaffective disorder, other disorders with co-morbid depression, and/or as a stand-alone treatment for major depressive disorder. We believe ITI-007 may also be useful for the treatment of bipolar disorder and other psychiatric and neurodegenerative disorders, particularly behavioral disturbances associated with dementia, autism and other CNS diseases.

We believe these features of ITI-007 may be able to improve the quality of life of patients with schizophrenia and enhance social function to allow them to integrate more fully into their families and their

## **Table of Contents**

workplaces. In addition, ITI-007 may be shown to treat disorders at either low-doses (*e.g.*, sleep, aggression and agitation) or high-doses (*e.g.*, acute exacerbated and residual schizophrenia, bipolar disorders, and mood disorders).

### *Phase 1 studies to support multiple clinical indications*

We conducted a series of Phase 1 safety studies of ITI-007 in Europe and the United States during the period from 2007 to 2011. All of the studies conducted to date in the United States have been conducted under an Investigational New Drug application, or IND, filed in 2007 by ITI. Data from these studies are being used to support the clinical development of ITI-007 in multiple indications, including schizophrenia, sleep disorders in neuropsychiatric and neurodegenerative disease, major depressive disorders, bipolar disorders, behavioral disturbances in dementia and Alzheimer's disease, autism, posttraumatic stress disorder, or PTSD, and intermittent explosive disorder, or IED. We have completed the following three Phase 1 trials in healthy volunteers:

A Phase 1, double-blind placebo controlled, single ascending dose study in 40 healthy volunteers in Europe in 2007. ITI-007 was generally well tolerated at all doses. Most adverse events, or AEs, were mild to moderate and all treatment related AEs resolved. The most frequent AE was headache.

A Phase 1, placebo controlled multiple ascending dose study in 25 healthy volunteers in Europe from 2007 to 2008. ITI-007 was generally well tolerated at all doses. Most AEs were mild to moderate and all treatment related AEs resolved.

A Phase 1, open-label positron emission tomography, or PET, study to demonstrate receptor occupancy, safety, tolerability and pharmacokinetics after single oral dose administration of ITI-007 in 16 healthy male volunteers. This study was conducted in the United States from 2007 to 2009. ITI-007 was well tolerated, all AEs were of mild or moderate intensity and all treatment related AEs resolved. Dose related increases in receptor occupancy at dopamine D2 receptors in the striatum were demonstrated after ITI-007 administration. Brain occupancy at 5-HT<sub>2A</sub> and serotonin reuptake transporters also was demonstrated after single doses of ITI-007.

We continued Phase 1 development of ITI-007 in patients with schizophrenia in order to advance ITI-007 in this target therapeutic indication. Specifically, we conducted the following additional studies:

A Phase 1b/2, placebo controlled multiple ascending dose study in 45 patients with stable schizophrenia in the United States during 2009 to 2010. ITI-007 was generally well tolerated at all doses. All AEs were mild to moderate and all treatment related AEs resolved. The overall percentage of patients reporting treatment related AEs was similar for those treated with ITI-007 (83.3% to 100%, across dose groups) and placebo (72.7%). The majority of the treatment related AEs that occurred at the commencement of the study decreased in terms of frequency and/or severity with repeated administration. We observed signs consistent with clinical efficacy in stable patients with schizophrenia in this study.

A Phase 1, randomized study to determine the tolerability, safety and pharmacokinetics of ITI-007 using different dosing regimens in 11 patients with schizophrenia. This study was conducted in the United States

in 2011. In this study, we showed that administration of ITI-007 in a capsule dosage form taken with food reduced the incidence of treatment related AEs and all treatment related AEs resolved. The most commonly reported treatment related AE in this study was somnolence, commonly known as drowsiness.

*ITI-007 for the treatment of exacerbated and residual schizophrenia*

In multiple clinical trials of ITI-007 in patients with schizophrenia, the drug candidate has demonstrated clinical signals consistent with reductions in psychosis, depression and insomnia. Reductions in psychosis are consistent with the potential to treat acute schizophrenia, whereas reductions in depression and insomnia are

---

**Table of Contents**

consistent with the potential to treat residual phase schizophrenia. ITI-007 has been shown to be safe and well-tolerated across a wide range of doses in these studies. Further, at doses that have demonstrated clinical activity, ITI-007 has caused fewer adverse effects than those typically associated with antipsychotic drug treatment, such as impaired motor function. These adverse side effects can be a major cause of patient noncompliance with current antipsychotic therapies and can lead to poorer social function.

**Phase 2 Clinical Trial (ITI-007-005)**

ITI-007 exhibited antipsychotic efficacy in ITI-007-005, a randomized, double-blind, placebo and active controlled Phase 2 clinical trial in patients with an acutely exacerbated episode of schizophrenia. In December 2013, we announced the clinical results from this Phase 2 trial. In this Phase 2 trial, 335 patients were randomized to receive one of four treatments: 60 mg of ITI-007, 120 mg of ITI-007, 4 mg of risperidone (active control) or placebo in a 1:1:1:1 ratio. Patients received study treatment orally once daily in the morning for 28 days. Of those randomized, 311 patients were included in the intent-to-treat primary analysis. Subject participation lasted approximately 7 to 8 weeks, including a one week screening period, a four week treatment period followed by stabilization on standard of care, and a safety follow up visit approximately two weeks after stabilization. The primary endpoint for this clinical trial was change from baseline to Day 28 on the PANSS total score. The PANSS is a well-validated 30-item rating scale that measures the ability of a drug to reduce schizophrenia symptom severity. The PANSS measures positive symptoms, such as delusions, suspiciousness, and hallucinations; negative symptoms, such as blunted affect, social and emotional withdrawal, and stereotyped thinking; and general psychopathology, such as anxiety, tension, depression, and active social avoidance.

Secondary endpoints in this trial included weekly assessments of the PANSS total score as well as its subscales (Positive Symptom Subscale, Negative Symptom Subscale, and General Psychopathology Subscale) and the Negative Symptom Factor (based on a subset of PANSS questions), individual item response on the PANSS, and the Calgary Depression Scale for Schizophrenia. Safety and tolerability were also assessed.

In December 2013, we announced that topline results from the ITI-007-005 study indicated that ITI-007 met the trial's pre-specified primary endpoint, improving symptoms associated with schizophrenia as measured by a statistically significant and clinically meaningful decrease in the PANSS total score. The trial also met key secondary outcome measures related to efficacy on PANSS subscales and safety.

Many patients with schizophrenia have deficits in social function. Social function is the ability to recognize, understand, process and use external cues to solve problems, maintain work performance and conduct interpersonal relationships. Deficits in social function often remain after positive symptoms, such as hallucinations and delusions, have resolved in these patients. In the Phase 2 trial, ITI-007 exhibited a differentiating response profile across a broad range of symptoms that we believe is consistent with improvements in these social functioning deficits. The study also showed that ITI-007 was well-tolerated at the tested doses. ITI-007 demonstrated a favorable safety profile in the study without characteristic antipsychotic drug side effects or any serious adverse events.

ITI-007 at a dose of 60 mg demonstrated a statistically significant improvement in psychosis ( $p = 0.017$ ) on the trial's pre-specified primary endpoint, which was change from baseline on the PANSS total score, compared to placebo. The primary statistical analysis was pre-specified and used a Mixed-Effect Model Repeated Measure method for handling missing data in the intent-to-treat, or ITT, study population and a Bonferroni procedure to correct for multiple two-sided comparisons (each dose of ITI-007 compared to placebo). The trial's pre-specified sensitivity analysis on the primary endpoint used the analysis of covariance, or ANCOVA, model and last observation carried forward, or LOCF, method for handling missing data for the ITT population and confirmed the positive outcome with statistically significant improvements compared to placebo in patients receiving the 60 mg dose of ITI-007 ( $p = 0.011$ ). ITI-007 at



a dose of 60 mg also significantly improved the positive symptom subscale ( $p < 0.05$ ) and the general psychopathology subscale ( $p < 0.05$ ) on the PANSS after 28 days of treatment using the ANCOVA-LOCF on the ITT population.

---

**Table of Contents**

The improvement in the PANSS total score in the 120 mg dose group did not reach statistical significance. We believe that it is possible that sedation, the most frequent side effect in the 120 mg dose group, interfered with the ability to detect an efficacy signal at this dose administered once daily in the morning. Approximately 32.5% of subjects randomized to 120 mg of ITI-007 experienced sedation/somnolence, compared to 21% of subjects randomized to risperidone, 17% of subjects randomized to 60 mg of ITI-007, and 13% randomized to placebo. We believe that nighttime administration may be more appropriate for testing the effectiveness of the 120 mg dose of ITI-007 in this patient population. In the trial, the 60 mg dose of ITI-007 was effective when administered once daily in the morning.

Consistent with preliminary indications from the interim analysis and with the drug candidate's pharmacological profile, ITI-007 at a dose of 60 mg significantly improved certain items on the negative symptom and general psychopathology subscales consistent with improved social function. The study was statistically powered only on the primary endpoint. ITI-007 did significantly improve many secondary endpoints, although the study was not designed for significance on secondary endpoints and was not powered to detect statistical differences in subgroup analyses.

A high percentage (74%) of randomized subjects completed trial participation. Only 19% of subjects discontinued from study treatment during the 28 day study treatment period, and an additional 7% of subjects completed study treatment but were lost to follow up.

In the Phase 2 trial, ITI-007 was well-tolerated. The most frequent AE was sedation, as described above. There were no serious adverse events related to ITI-007. There were no clinically meaningful changes in safety measures with ITI-007. Notably, ITI-007 demonstrated a favorable metabolic profile with no increase of blood levels of glucose, insulin, cholesterol or triglycerides over a four week treatment period. Moreover, in contrast to risperidone, 60 mg of ITI-007 was effective with no difference from placebo on weight change parameters, prolactin levels, extrapyramidal symptoms (EPS) or akathisia. ITI-007 was not associated with EPS as measured by the Simpson-Angus Scale, Barnes Akathisia Rating Scale, or Abnormal Involuntary Movement Scale. There was no increase in suicidal ideation or behavior with ITI-007.

**Phase 3 Clinical Trials and Regulatory Plans**

We are proceeding with Phase 3 development of ITI-007 for the treatment of schizophrenia. We are conducting two randomized, double-blind, placebo-controlled Phase 3 clinical trials of ITI-007 in patients with acutely exacerbated schizophrenia. In September 2015, we announced top-line clinical results from our first Phase 3 clinical trial of ITI-007 for the treatment of patients with schizophrenia. This randomized, double-blind, placebo-controlled Phase 3 clinical trial was conducted at 12 sites in the United States with 450 patients randomized (1:1:1) to receive either 60 mg of ITI-007, 40 mg of ITI-007 or placebo once daily in the morning for 28 days. The pre-specified primary efficacy measure was change from baseline versus placebo at study endpoint (4 weeks) on the centrally rated Positive and Negative Syndrome Scale, or PANSS, total score. In this trial, the once-daily dose of 60 mg of ITI-007 met the primary endpoint and demonstrated antipsychotic efficacy with statistically significant superiority over placebo at week 4 (study endpoint) with additional improvements observed in social function. Moreover, the 60 mg dose of ITI-007 showed significant antipsychotic efficacy as early as week 1, which was maintained at every time point throughout the entire study. ITI-007 showed a dose-related improvement in symptoms of schizophrenia with the 40 mg dose approximating the trajectory of improvement seen with the 60 mg dose, but the effect with 40 mg did not reach statistical significance on the primary endpoint. In addition, the 60 mg dose of ITI-007 met the key secondary endpoint of statistically significant improvement on the Clinical Global Impression Scale for Severity of Illness, or CGI-S. The 40 mg dose of ITI-007 also demonstrated a statistically significant improvement versus placebo on the CGI-S, though not formally tested against placebo since it did not separate on the primary endpoint. Consistent with previous studies, ITI-007 had a favorable safety and tolerability profile as evidenced by motoric, metabolic, and cardiovascular characteristics similar to placebo, and no clinically significant changes in akathisia, extrapyramidal

symptoms, prolactin, body weight, glucose, insulin, or lipids. We are also conducting a second Phase 3 clinical trial in schizophrenia that we initiated in the second quarter of 2015, with over 600 patients

---

**Table of Contents**

planned to be enrolled in the trial. In this trial, we are randomizing patients to two doses of ITI-007 (60 mg or 20 mg), risperidone (active control) or placebo over a 6-week treatment duration, and the primary outcome measure is change from baseline to Day 42 on the PANSS total score. We expect patient enrollment will be completed in the second quarter of 2016. Subject to timely enrollment, we anticipate top-line results from the second Phase 3 clinical trial will be available in mid-2016.

In addition to our Phase 3 clinical trials, we will need to complete other clinical and non-clinical trials and manufacturing and pre-commercialization activities necessary to support the submission of a planned NDA for ITI-007 in schizophrenia, which we currently expect could occur in the first half of 2017. Additional meetings with the FDA may be requested, as needed, to discuss in greater detail our plans for schizophrenia, and other elements of our regulatory strategy, including additional therapeutic indications, as the program progresses. Our clinical plans may change based on any discussions with the FDA, the relative success and cost of our research, preclinical and clinical development programs, whether we are able to enter into future collaborations, and any unforeseen delays or cash needs. If the FDA does not agree with our clinical development plans for ITI-007, our development of ITI-007 may be delayed and the costs of our development of ITI-007 could increase, which would have a material adverse effect on our business, financial condition and results of operations.

We are also developing long acting injectable formulations of ITI-007 for the treatment of schizophrenia. This is a pre-clinical stage development program.

**PET study of ITI-007 in patients with stable schizophrenia**

On September 16, 2015, we announced top-line data from an open-label positron emission tomography, or PET, study of ITI-007 examining brain occupancy of striatal D<sub>2</sub> receptors. This study was conducted in patients diagnosed with schizophrenia who were otherwise healthy and stable with respect to their psychosis. After washout from their previous antipsychotic medication for at least two weeks, PET was used to determine target occupancy in brain regions at baseline (drug-free) and again after two weeks of once daily ITI-007 oral administration. In this trial, the 60 mg dose of ITI-007 was associated with a mean of approximately 40% striatal dopamine D<sub>2</sub> receptor occupancy. As predicted by preclinical and earlier clinical data, ITI-007 demonstrated antipsychotic effect at relatively low striatal D<sub>2</sub> receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D<sub>2</sub> receptors. We believe this mechanism likely contributes to the favorable safety profile of ITI-007, with reduced risk for hyperprolactinemia, akathisia, extrapyramidal symptoms, and other motoric side effects.

***ITI-007 for the treatment of depressive episodes associated with bipolar disorder (bipolar depression)***

The pharmacological profile of ITI-007 offers the potential to treat bipolar mania, depression, and mixed symptoms at doses similar to those targeted for the treatment of schizophrenia. We believe that ITI-007 may be effective alone or in combination with mood stabilizers. Given that many patients with bipolar disorder also experience disturbed sleep and cognitive impairment similar to that observed in schizophrenia, we believe that ITI-007 may treat a wide array of symptoms in patients with bipolar disorder, including improvement of cognition and sleep.

Our bipolar depression program consists of two Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials: one to evaluate ITI-007 as a monotherapy and the other to evaluate ITI-007 as an adjunctive therapy with lithium or valproate. In each trial, approximately 550 patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode will be randomized to receive one of three treatments: 60 mg ITI-007, 40 mg ITI-007, or placebo in a 1:1:1 ratio orally once daily for 6 weeks. In the

ITI-007-401 trial, patients will receive ITI-007 or placebo as a monotherapy. In the ITI-007-402 trial, patients will receive ITI-007 or placebo adjunctive to their existing mood stabilizer lithium or valproate. We initiated our bipolar depression program in the third quarter of 2015.

The primary endpoint for both clinical trials is change from baseline at Day 42 on the Montgomery-Åsberg Depression Rating Scale (MADRS) total score versus placebo. The MADRS is a well-validated 10-item checklist that measures the ability of a drug to reduce overall severity of depressive symptoms. Individual items are rated

---

**Table of Contents**

by an expert clinician on a scale of 0 to 6 in which a score of 6 represents the most depressed evaluation for each item assessed. The total score ranges from 0 to 60. Secondary endpoints include measures of social function and quality of life that may illustrate the differentiated clinical profile of ITI-007. Safety and tolerability are also assessed in both clinical trials.

*ITI-007 for the treatment of behavioral disturbances associated with dementia, including Alzheimer's disease*

Behavioral disturbances are common in dementia and Alzheimer's disease. These disturbances are a major component of the burden to caregivers, and often lead to institutionalization. Although currently available treatments for patients with dementia mainly address cognitive disturbances, behavioral disturbances are considerably more problematic and likely more amenable to drug treatment. Several behavioral symptoms are quite prevalent in patients with dementia, including patients with Alzheimer's disease. In the fourth quarter of 2014, we announced the top-line data from ITI-007-200, a Phase 1/2 clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of ITI-007 in healthy geriatric subjects and in patients with dementia, including Alzheimer's disease. The ITI-007-200 clinical trial was conducted in two parts. Part 1 was a randomized, double-blind, placebo-controlled multiple ascending dose evaluation of ITI-007 in healthy geriatric subjects. In each of three cohorts in Part 1, approximately 10 subjects were randomized to receive ITI-007 (N=8) or placebo (N=2) orally once daily in the morning for seven days. Doses of ITI-007 up to and including 30 mg were evaluated in three cohorts in Part 1. In Part 2, eight patients with dementia were randomized to receive 9 mg ITI-007 (N=5) or placebo (N=3) orally once a day in the evening for seven days. The primary objectives of the study were to evaluate the safety, tolerability and pharmacokinetics of ITI-007 in the elderly and in the target dementia patient population. Secondary measures were included to explore the effects of ITI-007 on cognition and agitation. The Hopkins Verbal Learning Test-R, or HVLTR, was used to assess cognition in healthy geriatric subjects and dementia patients. The results demonstrated impaired verbal learning and memory (recall and recognition memory) by dementia patients relative to healthy geriatric subjects. Moreover, the data indicated that healthy geriatric subjects treated with ITI-007 for approximately one week experienced an improvement in verbal learning and memory relative to placebo-treated subjects. Dementia patients treated with ITI-007 showed enhanced recognition memory, making fewer false positive errors (i.e., responding yes to non-target words) than patients treated with placebo. Other secondary endpoints in the ITI-007-200 clinical trial included the assessment of agitation. However, none of the study participants experienced agitation at baseline or during the study, and therefore no signals on this behavioral endpoint could be assessed. The completion of this study marks an important milestone in our strategy to develop low doses of ITI-007 for the treatment of behavioral disturbances associated with dementia and related disorders. The ITI-007-200 trial results to date indicate that ITI-007 is safe and well-tolerated across a range of low doses, has linear- and dose-related pharmacokinetics and improves cognition in the elderly. The most frequent adverse event was mild sedation at the higher doses. We believe these results further position ITI-007 as a development candidate for the treatment of behavioral disturbances in patients with dementia and other neuropsychiatric and neurological conditions. We plan to initiate additional clinical programs evaluating ITI-007 in patients with behavioral disturbances associated with dementia and related disorders, including Alzheimer's disease, in the first half of 2016.

*ITI-007 for the treatment of sleep disturbances associated with neurologic and psychiatric disorders*

A Phase 2 double-blind, placebo controlled cross-over clinical trial conducted in 19 patients with primary insomnia with disturbed sleep maintenance at low doses of ITI-007 was completed in 2008 in Europe. The primary outcome measure was slow wave sleep as determined by polysomnography. ITI-007 demonstrated a dose-related statistically significant increase in slow wave sleep. Secondary measures were consistent with improvement of sleep maintenance in patients with primary insomnia, indicated by decreased waking after sleep onset, increased total sleep time, and no increase in latency to sleep onset. At these low doses ITI-007 did not induce sleep, but rather helped maintain sleep once sleep had been initiated. In addition, ITI-007 was not associated with next day cognitive impairment, or

hang-over effects. We believe that ITI-007 may be particularly useful in the treatment of sleep disorders that accompany neuropsychiatric and neurologic disorders, including schizophrenia, autism spectrum disorder, or ASD, Parkinson's disease and dementia. Previous work

---

**Table of Contents**

has suggested that selective 5-HT<sub>2A</sub> receptor antagonists increase deep, slow wave sleep in both humans and animals. We believe, however, that other neuropharmacological mechanisms, in addition to 5-HT<sub>2A</sub> receptor antagonism, such as engaging some dopamine modulation, may be beneficial for the successful treatment of sleep maintenance insomnia, or SMI, in humans. We believe that ITI-007 represents a new approach to the treatment of sleep maintenance insomnia because of its unique pharmacology and neuropharmacological interactions beyond selective 5-HT<sub>2A</sub> receptor antagonism. We believe that ITI-007 offers a potentially new approach to the treatment of sleep maintenance disorders, particularly in those disorders that accompany neuropsychiatric and neurologic disorders. Many of these disorders are accompanied by profound sleep deficits, which impair daytime functioning including cognition, exacerbate disease symptoms and increase the cost of care. We are presently exploring clinical designs to incorporate the examination of sleep disturbances in one or more of these indications. There is no assurance that any such design would be sufficient for an FDA approval for this indication.

*ITI-007 for the treatment of sleep and behavioral disturbances associated with autism spectrum disorder*

Sleep problems are common in patients with ASD and are not adequately treated by currently available interventions. Approximately two thirds of children and adolescents with ASD experience sleep problems, higher than the rate of sleep problems in age-matched developmentally typical children. Moreover, individuals with ASD suffer from behavioral disturbances, including aggression, irritability, anxiety and depression. With its multiple pathway mechanism of action, we believe that ITI-007 could address the multi-faceted behavioral symptoms associated with ASD. 5-HT<sub>2A</sub> receptor antagonism is predicted to increase slow wave sleep, improve sleep maintenance and reduce aggression. D<sub>2</sub> receptor modulation is predicted to improve sleep maintenance and reduce irritability and aggression. Serotonin reuptake inhibition is predicted to reduce anxiety and depression. Accordingly, we believe that ITI-007 could improve sleep maintenance, reduce behavioral disturbances and enhance social interaction in patients with ASD. We believe that our completed Phase 1 studies support advancing ITI-007 into Phase 2 trials in this patient population, and we are presently exploring the feasibility of such trials.

*ITI-007 for the treatment of depression and other mood disorders*

As a potent 5-HT<sub>2A</sub> receptor antagonist and serotonin reuptake inhibitor, we believe that ITI-007 could improve symptoms of depression with fewer side effects than selective serotonin reuptake inhibitors, or SSRIs. Dopamine modulation by ITI-007 may reduce irritability and aggression that can accompany many mood disorders. As such, ITI-007 may be effective for the treatment of mood disorders including MDD, PTSD, and IED. We are presently exploring the feasibility of clinical studies in these indications.

***ITI-002 (PDE1) Program***

We have a second major program called ITI-002 that has yielded a portfolio of compounds that selectively inhibits the enzyme phosphodiesterase type 1, or PDE1. We believe PDE1 helps regulate brain activity related to cognition, memory processes and movement/coordination. In addition, PDE1 inhibitors may have utility in treating non-CNS disorders. On February 25, 2011, we (through our wholly owned operating subsidiary, ITI) and Takeda Pharmaceutical Company Limited, or Takeda, entered into a license and collaboration agreement, or the Takeda License Agreement, under which we agreed to collaborate to research, develop and commercialize our proprietary compound ITI-214 and other selected compounds that selectively inhibit PDE1 for use in the prevention and treatment of human diseases. Takeda conducted four Phase 1 studies. A single rising dose study was conducted in the U.S. in healthy male and female, Japanese and non-Japanese volunteers. In a second U.S. study, ITI-214 was administered once daily over 14 days to healthy volunteers and patients with stable schizophrenia. In a third study, conducted in Japan, ITI-214 was administered for seven days at multiple rising oral doses in both male and female healthy volunteers. A fourth study compared the relative bioavailability of oral formulations of ITI-214 used in all previous



studies to an immediate-release tablet, either with or without food in healthy volunteers. In these studies, ITI-214 demonstrated a favorable safety profile and was generally

---

**Table of Contents**

well-tolerated across a broad range of doses both in healthy volunteers and in patients with schizophrenia with a pharmacokinetic profile that supports once daily dosing. ITI-214 is the first compound in its class to successfully advance into Phase 1 clinical trials. On October 31, 2014, we entered into an agreement with Takeda terminating the Takeda License Agreement, or the Termination Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. On September 15, 2015, Takeda completed the transfer of the Investigational New Drug application, or IND, for ITI-214 to us. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's disease, cognition in Alzheimer's disease, cognition in schizophrenia and in other non-CNS indications. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

***Additional PDE Programs***

There are multiple forms and isoforms of PDE with distinct roles in intracellular signaling. We have developed strong internal expertise in the design and synthesis of inhibitors specific for individual PDE isoforms. Based on our understanding of the expression and functions of these isoforms in the CNS, we have identified PDE2 and PDE9 as compelling targets for drug discovery. We believe that inhibitors of these PDEs may be useful in treating neurodegeneration and bioenergetic failure in a variety of CNS diseases.

**Intellectual Property*****Our Patent Portfolio***

As of February 1, 2016, we owned or controlled approximately 70 patent families filed in the United States and other major markets worldwide, including approximately 54 issued or allowed U.S. patents, 41 pending U.S. patent applications, 214 issued foreign patents, and 194 pending foreign patent applications, directed to novel compounds, formulations, methods of treatment, synthetic methods, and platform technologies.

Our ITI-007 program on novel compounds for neuropsychiatric and neurodegenerative diseases includes patents exclusively in-licensed from Bristol-Myers Squibb on families of compounds, including the ITI-007 lead molecule. We have extensively characterized this lead and filed additional patent applications on polymorphs, formulations, additional indications, derivatives and additional compounds. The ITI-007 lead molecule has composition of matter protection through 2025 and additional Orange Book-listable protection to 2034. Additionally, we expect to have data exclusivity in the European Union for up to 11 years from commercial launch. We also have a follow-on program, directed to compounds structurally related to the ITI-007 lead, but having composition of matter protection beyond 2031.

Our program on PDE1 inhibitors for cognition and dopamine-mediated disorders, such as Parkinson's disease, includes patent protection for the lead molecule, ITI-214, as well as a wide range of filings on other proprietary compounds and indications. The ITI-214 lead molecule has composition of matter protection to 2029, with possible extensions and additional Orange Book-listable protection to 2034. Additionally, we expect to have data exclusivity in the European Union for up to 11 years from commercial launch. We are also evaluating potential follow-on compounds for ITI-214 which would have patent protection beyond 2030.

We have also filed patent applications on novel proprietary targets and lead compounds for Alzheimer's disease, which would provide compound protection beyond 2028 or beyond 2034, depending on which compound is ultimately selected for development.

***License Agreement***

*The Bristol-Myers Squibb License Agreement*

On May 31, 2005, we entered into a worldwide, exclusive License Agreement with Bristol-Myers Squibb Company, or BMS, pursuant to which we hold a license to certain patents and know-how of BMS relating to ITI-007 and other specified compounds. The agreement was amended on November 3, 2010. The licensed rights are

## **Table of Contents**

exclusive, except BMS retains rights in specified compounds in the fields of obesity, diabetes, metabolic syndrome and cardiovascular disease. However, BMS has no right to use, develop or commercialize ITI-007 and other specified compounds in any field of use. We have the right to grant sublicenses of the rights conveyed by BMS. We are obliged under the license to use commercially reasonable efforts to develop and commercialize the licensed technology. We are also prohibited from engaging in the clinical development or commercialization of specified competitive compounds.

Under the agreement, we made an upfront payment of \$1.0 million to BMS, a milestone payment of \$1.25 million in December 2013, and a milestone payment of \$1.5 million in December 2014 following the initiation of our first Phase 3 clinical trial for ITI-007 for patients with exacerbated schizophrenia. Possible milestone payments remaining total \$12.0 million. Under the agreement, we may be obliged to make other milestone payments to BMS for each licensed product of up to an aggregate of approximately \$14.75 million. We are also obliged to make tiered single digit percentage royalty payments on sales of licensed products. We are obliged to pay to BMS a percentage of non-royalty payments made in consideration of any sublicense.

The agreement extends, and royalties are payable, on a country-by-country and product-by-product basis, through the later of ten years after first commercial sale of a licensed product in such country, expiration of the last licensed patent covering a licensed product, its method of manufacture or use, or the expiration of other government grants providing market exclusivity, subject to certain rights of the parties to terminate the agreement on the occurrence of certain events. On termination of the agreement, we may be obliged to convey to BMS rights in developments relating to a licensed compound or licensed product, including regulatory filings, research results and other intellectual property rights.

## ***Collaboration Agreement***

### ***The Takeda Pharmaceutical License and Collaboration Agreement and Termination Agreement***

On February 25, 2011, we entered into a license and collaboration agreement with Takeda Pharmaceutical Company Limited under which we agreed to collaborate to research, develop and commercialize our proprietary compound ITI-214 and other selected compounds that selectively inhibit PDE1 for use in the prevention and treatment of human diseases. As part of the agreement, we assigned to Takeda certain patents owned by us that claim ITI-214 and granted Takeda an exclusive license to develop and commercialize compounds identified in the conduct of the research program that satisfy specified criteria. However, we retained rights to all compounds that do not meet the specified criteria and we continue to develop PDE1 inhibitors outside the scope of the agreement. Upon execution of the agreement, Takeda made a nonrefundable payment to us.

Under the terms of the agreement, we conducted a research program with an initial term of three years to identify and characterize compounds that meet certain specified criteria sufficient for further development by Takeda. This research program ended in February 2014. We were responsible for our expenses incurred in the conduct of certain research activities specified in the research plan. Takeda agreed to reimburse us for expenses we incurred in conducting additional research activities.

On October 31, 2014, we entered into an agreement with Takeda terminating the Takeda License Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. On September 15, 2015, Takeda completed the transfer of the Investigational New Drug application, or IND, for ITI-214 to us. ITI-214 is the first compound in its class to successfully advance into Phase 1 clinical trials. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's disease, cognition in Alzheimer's disease, cognition in schizophrenia and in other non-CNS

indications. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

## **Table of Contents**

### **Manufacturing**

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, active pharmaceutical ingredient, or API, and finished product for our preclinical research and clinical trials, including the Phase 3 trials for ITI-007 for the treatment of schizophrenia and the treatment of bipolar depression. We believe that we would be able to contract with other third-party contract manufacturers to obtain API if our existing sources of API were no longer available, but there is no assurance that API would be available from other third-party manufacturers on acceptable terms, on the timeframe that our business would require, or at all. We do not have long-term agreements with our existing third-party contract manufacturers. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates if they are approved. As ITI-007 and any of our other product candidates continue to progress towards potential regulatory approval, we intend to enter into agreements with a third-party contract manufacturer and one or more back-up manufacturers for the commercial production of those products. Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our manufacturing contractors.

### **Sales and Marketing**

We currently have no marketing, sales or distribution capabilities. In order to commercialize any of our product candidates, we must develop these capabilities internally or through collaboration with third parties. In selected therapeutic areas where we feel that our product candidates can be commercialized by a specialty sales force that calls on a limited and focused group of physicians, we may plan to participate in the commercialization of our product candidates in the United States. In therapeutic areas that require a large sales force selling to a large and diverse prescribing population, we may elect to commercialize through, or in collaboration with, strategic partners. We may choose to commercialize our products in markets outside of the United States by establishing one or more strategic alliances in the future.

### **Competition**

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the United States and abroad. We compete, or will compete, with existing and new products being developed by our competitors. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions that our research and development programs target.

Even if we are successful in developing our product candidates, the resulting products would compete with a variety of established drugs in the areas of our targeted CNS therapeutic indications. Our potential products for the treatment of schizophrenia and bipolar disorder would compete with, among other branded products, Abilify<sup>®</sup>, marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical; Fanapt<sup>®</sup>, marketed by Novartis Pharmaceuticals; Seroquel XR<sup>®</sup>, marketed by AstraZeneca; Invega<sup>®</sup>, marketed by Janssen; VRAYLAR<sup>®</sup>, marketed by Allergan, Rexulti<sup>®</sup> marketed by Otsuka Pharmaceutical and Latuda<sup>®</sup>, marketed by Sunovion. In addition, our product candidates, if approved, will compete with, among other generic antipsychotic products, haloperidol, risperidone, quetiapine, olanzapine and clozapine.

In addition, the companies described above and other competitors may have a variety of drugs in development or awaiting FDA approval that could reach the market and become established before we have a product to sell. Our

competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Many of our competitors are using technologies or methods different or similar to

## **Table of Contents**

ours to identify and validate drug targets and to discover novel small molecule drugs. Many of our competitors and their collaborators have significantly greater experience than we do in the following:

identifying and validating targets;

screening compounds against targets;

preclinical and clinical trials of potential pharmaceutical products; and

obtaining FDA and other regulatory clearances.

In addition, many of our competitors and their collaborators have substantially greater advantages in the following areas:

capital resources;

research and development resources;

manufacturing capabilities; and

sales and marketing.

Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved by the FDA or are in advanced development. We face competition from other companies, academic institutions, governmental agencies and other public and private research organizations for collaborative arrangements with pharmaceutical and biotechnology companies, in recruiting and retaining highly qualified scientific and management personnel and for licenses to additional technologies. Our competitors, either alone or with their collaborators, may succeed in developing technologies or drugs that are more effective, safer, and more affordable or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. Developments by others may render our product candidates or our technologies obsolete. Our failure to compete effectively could have a material adverse effect on our business.

## **Government Regulation**

### ***United States FDA Process***

The research, development, testing, manufacture, labeling, promotion, advertising, import and export, distribution and marketing, among other things, of drug products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic



Act, or the FDCA, and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, warning letters, fines, civil penalties, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

*Drug Approval Process.* None of our drug product candidates may be marketed in the United States until the drug has received FDA approval. Such approval can take many years to obtain and may be rejected by the FDA at a number of steps. The steps required before a drug may be marketed in the United States generally include the following:

completion of extensive pre-clinical laboratory tests, animal studies, and formulation studies in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;

submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;

performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each proposed indication;

**Table of Contents**

submission to the FDA of an NDA after completion of all clinical trials;

satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the API and finished drug product are produced and tested to assess compliance with current Good Manufacturing Practices, or cGMPs;

satisfactory completion of FDA inspections of clinical trial sites to assure that data supporting the safety and effectiveness of product candidates has been generated in compliance with Good Clinical Practices; and

FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Pre-clinical tests include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The conduct of the pre-clinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the conduct of the trial, such as whether human research subjects will be exposed to an unreasonable health risk. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. The FDA, sponsor or an Institutional Review Board, or IRB may place a study on hold at any time during development.

Clinical trials involve administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be provided to the FDA as part of a separate submission to the IND. Further, an IRB, for each medical center proposing to conduct the clinical trial must review and approve the study protocol and informed consent information for study subjects for any clinical trial before it commences at that center, and the IRB must monitor the study until it is completed. There are also requirements governing reporting of on-going clinical trials and clinical trial results to public registries. Study subjects must sign an informed consent form before participating in a clinical trial.

Clinical trials necessary for product approval typically are conducted in three sequential phases, but the phases may overlap.

Phase 1 usually involves the initial introduction of the investigational drug into a limited population, typically healthy humans, to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness.

Phase 2 usually involves trials in a limited patient population to (i) evaluate dosage tolerance and appropriate dosage; (ii) identify possible adverse effects and safety risks; and (iii) evaluate preliminarily the efficacy of the drug for specific targeted indications. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

Phase 3 trials, commonly referred to as pivotal studies, are undertaken in an expanded patient population at multiple, geographically dispersed clinical trial centers to further evaluate clinical efficacy and test further for safety by using the drug in its final form.

The FDA or an IRB may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. The FDA may approve an NDA for a product candidate, but require that the sponsor conduct additional clinical trials to further assess the drug after NDA approval under a post-approval commitment. Post-approval trials are typically referred to as Phase 4 clinical trials.

## **Table of Contents**

During the development of a new drug, sponsors are given an opportunity to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach an agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug. A sponsor may request a Special Protocol Assessment, or SPA, to reach an agreement with the FDA that the protocol design, clinical endpoints, and statistical analyses are acceptable to support regulatory approval of the product candidate with respect to effectiveness in the indication studied. If such an agreement is reached, it will be documented and made part of the administrative record, and it will be binding on the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining the safety or effectiveness of the product after clinical studies begin, or if the sponsor fails to follow the protocol that was agreed upon with the FDA. There is no guarantee that a study will ultimately be adequate to support an approval even if the study is subject to an SPA.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Assuming successful completion of the required clinical testing, the results of pre-clinical studies and of clinical studies, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. An NDA must be accompanied by a significant user fee, which is waived for the first NDA submitted by a qualifying small business. The NDA is subject to a sixty day acceptance period, and if sufficiently complete to permit substantive review, will be filed by FDA at the end of that period. For NDAs assigned a standard review designation, the FDA's goal is to complete its review 12 months from submission and for priority review NDAs, 8 months from submission. These goals can be extended by the FDA requests for additional information from the sponsor.

The testing and approval process requires substantial time, effort and financial resources. The FDA will review the NDA and may deem it to be inadequate to support approval, and we cannot be sure that any approval will be granted on a timely basis, if at all. The FDA may also refer the application to the appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee, but it typically follows such recommendations.

Before approving an NDA, the FDA inspects the facility or the facilities at which the drug and/or its active pharmaceutical ingredient is manufactured and will not approve the product unless the manufacturing is in compliance with cGMPs. If the FDA evaluates the NDA and the manufacturing facilities are deemed acceptable, the FDA may issue an approval letter, or in some cases a Complete Response Letter. The approval letter authorizes commercial marketing of the drug for specific indications. As a condition of NDA approval, the FDA may require post-marketing testing and surveillance to monitor the drug's safety or efficacy, or impose other conditions. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or additional clinical trial(s), and/or other

significant, expensive and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials is not always conclusive and the FDA may interpret data differently than we or our collaborators interpret data.

---

**Table of Contents**

Alternatively, the FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy to mitigate risks of the drug, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. Once the FDA approves a drug, the FDA may withdraw product approval if on-going regulatory requirements are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing, including Phase 4 clinical trials, and surveillance programs to monitor the safety effects of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs or other information.

*Post-Approval Requirements.* After a drug has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. In addition, certain changes to an approved product, such as adding new indications, making certain manufacturing changes, or making certain additional labeling claims, are subject to further FDA review and approval. Before a company can market products for additional indications, it must obtain additional approvals from the FDA, typically a new NDA. Obtaining approval for a new indication generally requires that additional clinical studies be conducted. A company cannot be sure that any additional approval for new indications for any product candidate will be approved on a timely basis, or at all.

If post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. In addition, holders of an approved NDA are required to (i) report certain adverse reactions to the FDA and maintain pharmacovigilance programs to proactively look for these adverse events; (ii) comply with certain requirements concerning advertising and promotional labeling for their products; and (iii) continue to have quality control and manufacturing procedures conform to cGMPs after approval. The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing facilities, which includes assessment of on-going compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. We intend to use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including recall of the product from the market or withdrawal of approval of the NDA for that drug.

*Patent Term Restoration and Marketing Exclusivity.* Depending upon the timing, duration and specifics of FDA approval of the use of our drugs, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the extension must be requested prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Data and market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first

applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may

## **Table of Contents**

not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct, or obtain a right of reference to all of the pre-clinical studies, adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

### ***Foreign Regulation***

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials and approval of foreign countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

### ***Pricing and Reimbursement***

In the United States and internationally, sales of products that we market in the future, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability of adequate coverage and reimbursement from third-party payors, such as state and federal governments, managed care providers and private insurance plans. Private insurers, such as health maintenance organizations and managed care providers, have implemented cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that govern the drugs and biologics that will be offered and the out-of-pocket obligations of member patients for such products. We may need to conduct pharmacoeconomic studies to demonstrate the cost-effectiveness of our products for formulary coverage and reimbursement. Even with such studies, our products may be considered less safe, less effective or less cost-effective than existing products, and third-party payors may not provide coverage and reimbursement for our product candidates, in whole or in part.

In addition, particularly in the United States and increasingly in other countries, we are required to provide discounts and pay rebates to state and federal governments and agencies in connection with purchases of our products that are reimbursed by such entities. It is possible that future legislation in the United States and other jurisdictions could be enacted to potentially impact reimbursement rates for the products we are developing and may develop in the future and could further impact the levels of discounts and rebates paid to federal and state government entities. Any legislation that impacts these areas could impact, in a significant way, our ability to generate revenues from sales of products that, if successfully developed, we bring to market.

Political, economic and regulatory influences are subjecting the health care industry in the United States to fundamental changes. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the health care system in ways that could significantly affect our future business. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act,



or collectively, the ACA, enacted in March 2010, substantially changes the way health care is financed by both governmental and private insurers. Among other cost containment measures, ACA establishes:

an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents;

## **Table of Contents**

a new Medicare Part D coverage gap discount program, in which pharmaceutical manufacturers who wish to have their drugs covered under Part D must offer discounts to eligible beneficiaries during their coverage gap period, or the donut hole; and

a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted, which, among other things, reduce Medicare payments to providers by up to 2% per fiscal year.

## ***Sales and Marketing***

The FDA regulates all advertising and promotion activities for products under its jurisdiction prior to and after approval, including standards and regulations for direct-to-consumer advertising, dissemination of off-label information, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to collect additional data or conduct additional pre-clinical studies and clinical trials. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patient. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

Outside the United States, our ability to market a product is contingent upon obtaining marketing authorization from the appropriate regulatory authorities. The requirements governing marketing authorization, pricing and reimbursement vary widely from country to country.

We may also be subject to various federal and state laws pertaining to health care fraud and abuse, including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. Due to the breadth of the statutory provisions, the absence of guidance in the form of regulations, and very few court decisions addressing industry practices, it is possible that our practices might be challenged under anti-kickback or similar laws. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented, for payment to third-party payors (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal health care programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties also may be imposed upon executive officers and

employees, including criminal sanctions against executive officers under the so-called responsible corporate officer doctrine, even in situations where the executive officer did not intend to violate the law and

## **Table of Contents**

was unaware of any wrongdoing. Given the penalties that may be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government was to allege or convict us or our executive officers of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing attention being given to them by law enforcement authorities. Further, there are an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. Given the lack of clarity in laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state authorities.

## **Description of the Merger**

Pursuant to an Agreement and Plan of Merger dated August 23, 2013, or the Merger Agreement, by and among Oneida Resources Corp., which we refer to as the Company, we, our and us; ITI, Inc., a Delaware corporation and wholly-owned subsidiary of the Company, or Merger Sub; and Intra-Cellular Therapies, Inc., a Delaware corporation, which we refer to as ITI; Merger Sub merged with and into ITI, with ITI remaining as the surviving entity and a wholly-owned operating subsidiary of the Company. This transaction is referred to throughout this report as the Merger. The Merger was effective on August 29, 2013, upon the filing of a Certificate of Merger with the Secretary of State of the State of Delaware. In connection with the Merger, ITI changed its name to ITI, Inc. and Oneida Resources Corp. assumed the name Intra-Cellular Therapies, Inc. The Merger was accounted for as a capital transaction. Upon the effectiveness of the Merger, the Company's business became the operation of ITI and its business.

At the effective time of the Merger, or the Effective Time, the legal existence of Merger Sub ceased and each share of ITI common stock and each share of ITI preferred stock that was issued and outstanding immediately prior to the Effective Time was automatically exchanged for 0.5 shares of our common stock, which we refer to as the Exchange. Immediately following the Effective Time, we completed the closing of a redemption of 5,000,000 shares of our common stock, or the Redemption, from our then-current sole stockholder, which constituted all of the issued and outstanding shares of our capital stock, on a fully-diluted basis, immediately prior to the Merger. Upon completion of the Merger and the Redemption, the former stockholders of ITI held 100% of the outstanding shares of our capital stock. Unless otherwise indicated in this report, all share and per share figures reflect the exchange of each share of ITI common stock and each share of ITI preferred stock then outstanding for 0.5 shares of our common stock at the Effective Time.

## **Employees**

As of February 15, 2016, we employed 39 employees, 37 of whom were full-time. We consider our relations with our employees to be good. To successfully develop our drug candidates, we must be able to attract and retain highly skilled personnel. We anticipate hiring additional employees for research and development, clinical and regulatory affairs and general and administrative activities over the next few years. In addition, we intend to use clinical research organizations and third parties to perform our clinical studies and manufacturing.

---

**Table of Contents****Item 1A. RISK FACTORS**

*Except for the historical information contained herein, this report contains forward-looking statements that involve risks and uncertainties. These statements include projections about our finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed in the following section, as well as those discussed in Part II, Item 7 entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this report.*

*You should consider carefully the following risk factors, together with all of the other information included or incorporated by reference in this report. If any of the following risks, either alone or taken together, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common stock could decline, and stockholders may lose all or part of their investment.*

**Risks Related to Our Business**

***We currently do not have, and may never have, any products that generate significant revenues.***

We have a limited operating history on which to evaluate our business and prospects. To date, we have not generated any product revenues from our product candidates currently in development. We cannot guarantee that any of our product candidates currently in development will ever become marketable products.

We must demonstrate that our drug candidates satisfy rigorous standards of safety and efficacy for their intended uses before the FDA and other regulatory authorities in the European Union and elsewhere will approve them for commercialization. Significant additional research, preclinical testing and clinical testing is required before we can file applications with the FDA or other regulatory authorities for premarket approval of our drug candidates. In addition, to compete effectively, our drugs must be easy to administer, cost-effective and economical to manufacture on a commercial scale. We may not achieve any of these objectives. In September 2015, we announced top-line results from our first Phase 3 clinical trial of our most advanced drug candidate, ITI-007, in schizophrenia. We also initiated enrollment of our second Phase 3 clinical trial of ITI-007 in schizophrenia in the second quarter of 2015 and, subject to timely enrollment, we anticipate that top-line results from this trial will be available in mid-2016. In addition, all rights with respect to ITI-214, which has advanced into Phase 1 clinical trials that we previously granted to Takeda were recently returned to us in connection with the termination of the Takeda License Agreement. On September 15, 2015, Takeda completed the transfer of the IND for ITI-214 to us. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's disease, cognition in Alzheimer's disease, cognition in schizophrenia and in other non-CNS indications. We cannot be certain that the clinical development of these or any other drug candidates in preclinical testing or clinical development will be successful, that we will receive the regulatory approvals required to commercialize them or that any of our other research and drug discovery programs will yield a drug candidate suitable for investigation through clinical trials. Our commercial revenues from our product candidates currently in development, if any, will be derived from sales of drugs that will not become marketable for several years, if at all.

***There is no guarantee that our planned clinical trials for ITI-007 in schizophrenia or in other indications will be successful.***

In our Phase 1 and Phase 2 clinical trials, our lead product candidate, ITI-007, has demonstrated improved sleep maintenance, antipsychotic efficacy, and clinical signals consistent with reduction in negative symptoms associated with schizophrenia, depression and anxiety, and other symptoms associated with impaired social

---

**Table of Contents**

function. In September 2015, we announced top-line clinical results from our first randomized, double-blind, placebo-controlled Phase 3 clinical trial in patients with an acutely exacerbated episode of schizophrenia. In this trial, a once-daily 60 mg dose of ITI-007 met the primary endpoint and demonstrated antipsychotic efficacy with statistically significant superiority over placebo at week 4 (study endpoint). In addition, the 60 mg dose of ITI-007 met the key secondary endpoint of statistically significant improvement on the CGI-S. We are currently planning confirmatory later-stage clinical trials and recently initiated enrollment of our second Phase 3 clinical trial of ITI-007 in schizophrenia in the second quarter of 2015. In addition, we initiated our bipolar depression program in the third quarter of 2015.

The historical rate of failures for product candidates in clinical development and late-stage clinical trials is high. While we plan to conduct further clinical trials in patients with schizophrenia and other indications, there is no guarantee that we will have the same level of success in these trials as we have had in our earlier clinical trials, or be successful at all.

In addition, although we believe that ITI-007 and follow-on compounds may also have clinical utility in indications other than schizophrenia, such as behavioral disturbances in dementia, bipolar disorder, intermittent explosive disorder, non-motor disorders associated with Parkinson's disease, obsessive compulsive disorder and anxiety disorders and post-traumatic stress disorder, we have never tested ITI-007 in Phase 2 clinical trials in the patient population for these other indications, except for ITI-007-200, a Phase 1/2 clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of ITI-007 in healthy geriatric subjects and in patients with dementia, including Alzheimer's disease, for which we announced top-line data in the fourth quarter of 2014.

If we do not successfully complete clinical development of ITI-007, we will be unable to market and sell products derived from it and to generate product revenues. Even if we do successfully complete clinical trials for ITI-007 in patients with schizophrenia, those results are not necessarily predictive of results of future pivotal trials that may be needed before we may submit an NDA to the FDA for the initial or other future indications. Of the vast number of drugs in development, only a small percentage result in the submission of an NDA to the FDA, and even less result in the NDA ultimately being approved by the FDA for commercialization.

***We have recently completed our first Phase 3 clinical trial of ITI-007 for the treatment of schizophrenia and are proceeding with our second Phase 3 clinical trial of ITI-007 for the treatment of schizophrenia. Although we have discussed our clinical development plans with the FDA, the agency may ultimately determine that our Phase 3 clinical trials and non-clinical studies, even if successfully completed, are not sufficient for regulatory approval. If we are required to conduct additional clinical trials and non-clinical studies, our development of ITI-007 for schizophrenia will be more time-consuming and costly than we presently anticipate, which would have a material adverse effect on our business, results of operations and financial condition.***

In June 2014, we held our end-of-Phase 2 meeting with the FDA to discuss our plans for initiating Phase 3 clinical trials of ITI-007 in schizophrenia. Following this meeting, we proceeded with our Phase 3 development program, in which we recently completed the first of two randomized, double-blind, placebo-controlled Phase 3 clinical trials of ITI-007 in patients with acutely exacerbated schizophrenia, with 450 patients enrolled in the first Phase 3 clinical trial and over 600 patients planned to be enrolled in the second Phase 3 clinical trial. We completed enrollment of the first Phase 3 clinical trial in schizophrenia in the second quarter of 2015 and initiated enrollment of the second Phase 3 clinical trial in schizophrenia in the second quarter of 2015. In the first Phase 3 trial, we randomized patients to two doses of ITI-007 (60mg or 40mg) or placebo over a 4-week treatment duration, and the primary outcome measure is change from baseline to Day 28 on the PANSS total score. In the second Phase 3 trial, we are randomizing patients to receive one of four treatments: 60 mg ITI-007, 20 mg ITI-007, 4 mg risperidone (active control) or placebo in a 1:1:1:1 ratio. The second Phase 3 trial is being conducted for a 6-week treatment duration. We announced top-line

results of the first Phase 3 clinical trial of ITI-007 in patients with schizophrenia in September 2015 and anticipate that the results of the second Phase 3 clinical trial will be available, subject to timely enrollment, in mid-2016. Even though we believe that our recently completed Phase 3 trial and our on-going Phase 3 clinical trial and ongoing and planned clinical and



---

**Table of Contents**

non-clinical studies for ITI-007 in schizophrenia, if successful, will be sufficient to support our NDA, the FDA may not agree with one or more aspects of our clinical trial designs, including the duration of the trials, clinical endpoints, controls, dose ranges, collection of safety data, or adequacy of our non-clinical studies. If we submit an NDA and the FDA does not agree with our clinical and non-clinical designs, our development of ITI-007 in schizophrenia and other indications may be delayed, and we may incur additional costs and devote additional resources to address any concerns the FDA may have with our trial designs. In addition, we may be required to conduct additional clinical trials or studies, which could result in additional delays and costs. There is no assurance that we will complete the Phase 3 trials and other clinical and non-clinical studies within the timeframes and the costs that we currently expect, or at all, or in a manner that is acceptable to the FDA. Any delays or unplanned costs resulting from our Phase 3 clinical trials of ITI-007 in schizophrenia may have a material adverse effect on our business, results of operations and financial condition. Even if we eventually complete Phase 3 clinical testing, submit an NDA and receive approval of ITI-007, the FDA may grant approval contingent on the performance of costly additional post-approval clinical trials. The FDA may also approve ITI-007 for a more limited indication or a narrower patient population than we originally requested, and the FDA may not approve the labeling that we believe is necessary or desirable for the successful commercialization of ITI-007 or our other product candidates. Any delay in obtaining, or inability to obtain, applicable regulatory approval for ITI-007 would delay or prevent commercialization of ITI-007 and would materially adversely impact our business, results of operations and financial condition.

***We expect our net losses to continue for at least several years and are unable to predict the extent of future losses or when we will become profitable, if ever.***

We have experienced significant net losses since our inception. As of December 31, 2015, we had an accumulated deficit of approximately \$193.0 million. We expect to incur net losses over the next several years as we advance our programs and incur significant clinical development costs. We have not received, and do not expect to receive for at least the next several years, any revenues from the commercialization of our product candidates. Substantially all of our revenues to date were from our license and collaboration agreement with Takeda and our agreements with various U.S. governmental agencies and other parties, including our research and development grants. In October 2014, we entered into the Takeda Termination Agreement, which terminated our license and collaboration agreement with Takeda, pursuant to which all rights with respect to ITI-214 that we previously granted to Takeda were returned to us. We will not, therefore, receive any further milestone payments from Takeda and we cannot be certain that we will enter into additional collaboration agreements. To obtain revenues from our product candidates, we must succeed, either alone or with others, in developing, obtaining regulatory approval for, and manufacturing and marketing drugs with significant market potential. We may never succeed in these activities, and may never generate revenues that are significant enough to achieve profitability.

***We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not so available, may require us to delay, limit, reduce or cease our operations.***

We have consumed substantial amounts of capital since our inception. Our cash, cash equivalents and investment securities totaled \$475.2 million at December 31, 2015, which includes net proceeds of approximately \$121.8 million from the public offering of shares of our common stock in March 2015 and approximately \$327.4 million from the public offering of shares of our common stock in September 2015. While we believe that our existing cash, cash equivalents and investment securities, together with interest on cash balances, will be sufficient to fund our operating expenses and capital expenditure requirements through the end of 2018, the amount and timing of our actual expenditures will depend upon numerous factors, including the ongoing status of our second Phase 3 clinical trials of ITI-007 in patients with acute exacerbated schizophrenia and bipolar depression, the continued development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, and our other planned clinical and non-clinical trials. Furthermore, we anticipate that we will need to secure additional funding to obtain

regulatory approval for ITI-007 in patients with dementia, including Alzheimer's disease, for further development of ITI-007 in patients with bipolar disorder, depressive disorders and other indications, and for development of our other product candidates.

**Table of Contents**

If the FDA requires that we perform additional preclinical studies or clinical trials, or we experience delays or other setbacks in our clinical trials, our expenses would further increase beyond what we currently expect and the anticipated timing of any potential NDA would likely be delayed.

With the remaining proceeds from our public offerings in February 2014, March 2015 and September 2015, we intend to fund the following: the completion of two Phase 3 clinical trials of ITI-007 in patients with acute exacerbated schizophrenia, one of which we announced top-line results in September 2015 and the second of which we initiated enrollment in the second quarter of 2015; the initiation of other planned clinical and non-clinical trials, including manufacturing, needed for anticipated regulatory approval of ITI-007 in patients with acute exacerbated schizophrenia and other potential additional indications; pre-launch activities for ITI-007 for the treatment of schizophrenia and, if it receives regulatory approval, to fund our initial commercialization efforts; the completion of our clinical trials of ITI-007 in bipolar disorder as a monotherapy and as an adjunctive therapy with lithium or valproate, a program we initiated in the third quarter of 2015; clinical trials of ITI-007 for the treatment of behavioral disturbances in dementia; pre-clinical and clinical development of our ITI-007 long acting injectable development program; other clinical trials of ITI-007; the continued clinical development of our PDE1 program, including ITI-214; and research and preclinical development of our other product candidates and the continuation of manufacturing activities in connection with the development of ITI-007. The remaining proceeds, if any, will be used to fund new and ongoing research and development activities, new business opportunities, general corporate purposes, including general and administrative expenses, capital expenditures and working capital. Accordingly, we will continue to require substantial additional capital beyond the net proceeds from these offerings to continue our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds we will require to complete research and development and commercialize our products under development.

Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

the progress in, and the costs of, our preclinical studies and clinical trials and other research and development programs;

the scope, prioritization and number of our research and development programs;

the ability of any future collaborators and us to reach the milestones, and other events or developments, triggering payments under any future collaboration agreements or to otherwise make payments under such agreements;

our ability to enter into new, and to maintain any existing, collaboration and license agreements;

the extent to which any future collaborators are obligated to reimburse us for clinical trial costs under any future collaboration agreements;

the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;

the costs of securing manufacturing arrangements for clinical or commercial production;

the costs of preparing applications for regulatory approvals for our product candidates;

the costs of preparing for and establishing, or contracting for, sales and marketing capabilities if we obtain regulatory clearances to market our product candidates; and

the costs associated with litigation.

Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through our existing cash, cash equivalents and investment securities, strategic collaborations, private or public sales of our securities, debt financings, grant funding, or by licensing all or a portion of our product candidates or technology. Turmoil and volatility in the financial markets have adversely affected the market capitalizations of

---

**Table of Contents**

many biotechnology companies, and generally made equity and debt financing more difficult to obtain. This, coupled with other factors, may limit our access to additional financing. This could have a material adverse effect on our ability to access sufficient funding. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. If we do obtain additional funding through equity offerings, the ownership of our existing stockholders and purchasers of shares of our common stock in any such offering will be diluted, and the terms of any financing may adversely affect the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline. If funds are not available, we will be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. We also could be required to seek funds through arrangements with collaboration partners or otherwise that may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us.

***Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations.***

Our management has significant flexibility in applying our cash resources, including the net proceeds from our public offerings completed in February 2014, March 2015 and September 2015, and could use these resources for corporate purposes that do not increase our market value, or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which could adversely affect our future growth prospects.

***Our lead product candidate, ITI-007, is only part way through the clinical trials we anticipate needing to complete before we may be able to submit an NDA to the FDA. Clinical trials are long, expensive and unpredictable, and there is a high risk of failure.***

Preclinical testing and clinical trials are long, expensive and unpredictable processes that can be subject to delays. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a drug, and delays or failure can occur at any stage. Interim results of clinical trials do not necessarily predict final results, and success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials.

In connection with clinical trials, we face risks that a product candidate may not prove to be efficacious; patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested; the results may not confirm the positive results of our earlier preclinical studies and clinical trials; and the results may not meet the level of statistical significance required by the FDA or other regulatory agencies. If we do not successfully complete preclinical and clinical development, we will be unable to market and sell products derived from our product candidates and to generate product revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before an NDA may be submitted to the FDA or the FDA may approve the NDA.

***Delays, suspensions and terminations in our clinical trials could result in increased costs to us, delay our ability to generate product revenues and therefore may have a material adverse effect on our business, results of operations and future growth prospects.***

The commencement of clinical trials can be delayed for a variety of reasons, including delays in: demonstrating sufficient safety and efficacy to obtain regulatory approval to commence a clinical trial; reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites; manufacturing sufficient

quantities of a product candidate; obtaining clearance from the FDA to commence clinical trials pursuant to an IND; obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site; and patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

## **Table of Contents**

Once a clinical trial has begun, it may be delayed, suspended or terminated due to a number of factors, including: ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results; failure to conduct clinical trials in accordance with regulatory requirements; lower than anticipated screening or retention rates of patients in clinical trials; serious adverse events or side effects experienced by participants; and insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials.

Many of these factors may also ultimately lead to denial of regulatory approval of a current or potential product candidate. If we experience delays, suspensions or terminations in a clinical trial, our costs will increase, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed.

***Safety issues with our product candidates, or with product candidates or approved products of third parties that are similar to our product candidates, could give rise to delays in the regulatory approval process, restrictions on labeling or product withdrawal after approval.***

Problems with product candidates or approved products marketed by third parties that utilize the same therapeutic target or that belong to the same therapeutic class as our product candidates could adversely affect the development, regulatory approval and commercialization of our product candidates. In 2012, the FDA released draft guidance recommending that prospective suicidality assessments be performed in clinical trials of any drug being developed for a psychiatric indication. Our development programs are focused on psychiatric indications. Our PDE program is a novel target and may have unexpected safety effects that do not appear until late in clinical development or after commercial approval. To date, none of our product candidates have experienced any serious and unexpected suspected adverse reactions that resulted in the submission of an IND safety report to the FDA; however, some approved products marketed by third parties for psychiatric indications that utilize different therapeutic targets or are in a different therapeutic class have experienced significant safety issues. As we continue the development and clinical trials of our product candidates, there can be no assurance that our product candidates will not experience significant safety issues.

Discovery of previously unknown class effect problems may prevent or delay clinical development and commercial approval of product candidates or result in restrictions on permissible uses after their approval, including withdrawal of the medicine from the market. Many drugs acting on the CNS include boxed warnings and precautions related to suicidal behavior or ideation, driving impairment, somnolence/sedation and dizziness, discontinuation, weight gain, non-insulin dependent (type II) diabetes, cardiovascular side effects, sleep disturbances, and motor disturbances. If we or others later identify undesirable side effects caused by the mechanisms of action or classes of our product candidates or specific product candidates:

we may be required to conduct additional clinical trials or implement a Risk Evaluation and Mitigation Strategies program prior to or following approval;

regulatory authorities may not approve our product candidates or, as a condition of approval, require specific warnings and contraindications;

regulatory authorities may withdraw their approval of the product and require us to take our drug off the market;

we may have limitations on how we promote our drugs;

sales of products may decrease significantly;

we may be subject to litigation or product liability claims; and

our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase our commercialization costs and expenses, which, in turn, could delay or prevent us from generating significant revenues from its sale.



**Table of Contents**

Finally, if the FDA determines that a drug may present a risk of substance abuse, it can recommend to the Drug Enforcement Administration that the drug be scheduled under the Controlled Substances Act. Any failure or delay in commencing or completing clinical trials or obtaining regulatory approvals for our product candidates would delay commercialization of our product candidates, and severely harm our business and financial condition.

***If we seek to enter into strategic alliances for our drug candidates, but fail to enter into and maintain successful strategic alliances, we may have to reduce or delay our drug candidate development or increase our expenditures.***

An important element of a biotechnology company's strategy for developing, manufacturing and commercializing its drug candidates may be to enter into strategic alliances with pharmaceutical companies or other industry participants to advance its programs and enable it to maintain its financial and operational capacity. We may face significant competition in seeking appropriate alliances. If we seek such alliances, we may not be able to negotiate alliances on acceptable terms, if at all. In addition, these alliances may be unsuccessful. On October 31, 2014, we entered into the Termination Agreement with Takeda, which terminated the Takeda License Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. If we seek such alliances and then fail to create and maintain suitable alliances, we may have to limit the size or scope of, or delay, one or more of our drug development or research programs. If we elect to fund drug development or research programs on our own, we will have to increase our expenditures and will need to obtain additional funding, which may be unavailable or available only on unfavorable terms.

***To the extent we are able to enter into collaborative arrangements or strategic alliances, we will be exposed to risks related to those collaborations and alliances.***

Biotechnology companies at our stage of development sometimes become dependent upon collaborative arrangements or strategic alliances to complete the development and commercialization of drug candidates, particularly after the Phase 2 stage of clinical testing. If we elect to enter into collaborative arrangements or strategic alliances, these arrangements may place the development of our drug candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

Dependence on collaborative arrangements or strategic alliances would subject us to a number of risks, including the risk that:

we may not be able to control the amount and timing of resources that our collaborators may devote to the drug candidates;

our collaborators may experience financial difficulties;

we may be required to relinquish important rights, such as marketing and distribution rights;

business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement;

a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and

collaborative arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

***Preliminary and interim data from our clinical studies that we may announce or publish from time to time may change as more patient data become available.***

From time to time, we may announce or publish preliminary or interim data from our clinical studies. Preliminary and interim results of a clinical trial are not necessarily predictive of final results. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change as patient

**Table of Contents**

enrollment continues and more patient data become available. As a result, preliminary and interim data should be viewed with caution until the final data are available. Material adverse changes in the final data compared to the interim data could significantly harm our business prospects.

***We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing our product candidates.***

Although we design and manage our current preclinical studies and clinical trials, we do not now have the ability to conduct clinical trials for our product candidates on our own. In addition to our collaborators, we rely on contract research organizations, medical institutions, clinical investigators, and contract laboratories to perform data collection and analysis and other aspects of our clinical trials. In addition, we also rely on third parties to assist with our preclinical studies, including studies regarding biological activity, safety, absorption, metabolism, and excretion of product candidates.

Our preclinical activities or clinical trials may be delayed, suspended, or terminated if: the quality or accuracy of the data obtained by the third parties on whom we rely is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or if for other reasons, these third parties do not successfully carry out their contractual duties or fail to meet regulatory obligations or expected deadlines, or these third parties need to be replaced.

If the third parties on whom we rely fail to perform, our development costs may increase, our ability to obtain regulatory approval, and consequently, to commercialize our product candidates may be delayed or prevented altogether. We currently use several contract research organizations to perform services for our preclinical studies and clinical trials. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or incurring additional expenses.

***Even if we successfully complete the clinical trials of one or more of our product candidates, the product candidates may fail for other reasons.***

Even if we successfully complete the clinical trials for one or more of our product candidates, the product candidates may fail for other reasons, including the possibility that the product candidates will:

fail to receive the regulatory approvals required to market them as drugs;

be subject to proprietary rights held by others requiring the negotiation of a license agreement prior to marketing;

be difficult or expensive to manufacture on a commercial scale;

have adverse side effects that make their use less desirable; or

fail to compete with product candidates or other treatments commercialized by our competitors. If we are unable to receive the required regulatory approvals, secure our intellectual property rights, minimize the incidence of any adverse side effects or fail to compete with our competitors' products, our business, financial condition, and results of operations could be materially and adversely affected.

***Following regulatory approval of any of our drug candidates, we will be subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our potential products.***

With regard to our drug candidates, if any, approved by the FDA or by another regulatory authority, we are held to extensive regulatory requirements over product manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping. Regulatory approvals may also be subject to

**Table of Contents**

significant limitations on the indicated uses or marketing of the drug candidates. Potentially costly follow-up or post-marketing clinical studies may be required as a condition of approval to further substantiate safety or efficacy, or to investigate specific issues of interest to the regulatory authority. Previously unknown problems with the drug candidate, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

In addition, the law or regulatory policies governing pharmaceuticals may change. New statutory requirements may be enacted or additional regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or elsewhere. If we are not able to maintain regulatory compliance, we might not be permitted to market our drugs and our business could suffer.

***Our product candidates may not gain acceptance among physicians, patients, or the medical community, thereby limiting our potential to generate revenues, which will undermine our future growth prospects.***

Even if our product candidates are approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product candidate by physicians, health care professionals and third-party payors, and our profitability and growth will depend on a number of factors, including:

our ability to provide acceptable evidence of safety and efficacy;

pricing and cost effectiveness, which may be subject to regulatory control;

our ability to obtain sufficient third-party insurance coverage or reimbursement;

effectiveness of our or our collaborators' sales and marketing strategy;

relative convenience and ease of administration;

prevalence and severity of any adverse side effects; and

availability of alternative treatments.

If any product candidate that we develop does not provide a treatment regimen that is at least as beneficial as the current standard of care or otherwise does not provide some additional patient benefit over the current standard of care, that product will not achieve market acceptance and we will not generate sufficient revenues to achieve profitability.

***The failure to attract and retain skilled personnel and key relationships could impair our drug development and commercialization efforts.***

We are highly dependent on our senior management and key clinical development, scientific and technical personnel. Competition for these types of personnel is intense. The loss of the services of any member of our senior management, clinical development, scientific or technical staff may significantly delay or prevent the achievement of drug development and other business objectives and could have a material adverse effect on our business, operating results and financial condition. We also rely on consultants and advisors to assist us in formulating our strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us. We intend to expand and develop new drug candidates, and will need additional funding to grow our business. We will need to hire additional employees in order to continue our research and clinical trials and to market our drugs when approved. This strategy will require us to recruit additional executive management and clinical development, regulatory, scientific, technical and sales and marketing personnel. There is currently intense competition for skilled executives and employees with relevant clinical development, scientific, technical and sales and marketing expertise, and this competition is likely to continue. The inability to attract and retain sufficient clinical development, scientific, technical and managerial personnel, due to intense competition and our limited

## **Table of Contents**

resources, would limit or delay our product development efforts, which would adversely affect the development of our drug candidates and commercialization of our potential drugs and growth of our business.

***We may not be able to continue or fully exploit our partnerships with outside scientific and clinical advisors, which could impair the progress of our clinical trials and our research and development efforts.***

We work with scientific and clinical advisors at academic and other institutions who are experts in the field of CNS disorders. They advise us with respect to our clinical trials. These advisors are not our employees and may have other commitments that would limit their future availability to us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services, which may impair our reputation in the industry and delay the development or commercialization of our product candidates.

***Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale. In particular, we will need to develop a larger scale manufacturing process that is more efficient and cost-effective to commercialize ITI-007 and other product candidates, which may not be successful, and which may require us to transfer our production to one or more other third-party manufacturers, potentially delaying regulatory approval and commercialization.***

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of raw materials. There is no assurance that our manufacturers will be successful in establishing a larger-scale commercial manufacturing process for ITI-007 which achieves our objectives for manufacturing capacity and cost of goods. Even if we could otherwise obtain regulatory approval for any product candidate, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities of the approved product for commercialization, our commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

***We rely on third-party manufacturers to manufacture and supply our product candidates for us. If one of our suppliers or manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts to find new suppliers or manufacturers. We may also face significant delays in our clinical trials, regulatory approvals and product introductions and commercialization.***

We have no manufacturing facilities and have limited experience in the manufacturing of drugs or in designing drug-manufacturing processes. We have contracted with third-party manufacturers to produce, in collaboration with us, our product candidates, including ITI-007, for clinical trials. If any of our product candidates are approved by the FDA or other regulatory agencies for commercial sale, we may need to amend our contracts with our current manufacturers or contract with other third parties to manufacture them in larger quantities at commercial scale. While we believe that there are alternative sources available to manufacture our product candidates, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty but, if they were to occur, they could cause a delay in our development and commercialization efforts. We have not entered into a long-term agreement with our current third-party manufacturers or with any alternate suppliers. Although we intend to do so prior to any commercial launch of a product that is approved by the FDA in order to ensure that we maintain adequate supplies of commercial drug product, we may be unable to enter into such agreements or do so on commercially reasonable terms, which could delay a product launch or subject our commercialization efforts to significant supply risk.





---

**Table of Contents**

Manufacturers of our product candidates are obliged to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs. The manufacture of pharmaceutical products in compliance with the cGMPs requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced cGMP requirements, other federal and state regulatory requirements and foreign regulations. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our ability to provide product candidates in our clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial materials could delay the completion of our clinical trials, increase the costs associated with maintaining our clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at significant additional expense or terminate the clinical trials completely.

In addition, the facilities used by our contract manufacturers or other third party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we request regulatory approval from the FDA. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. We have little control over our manufacturers' compliance with these regulations and standards. A failure of any of our current or future contract manufacturers to establish and follow cGMPs and to document their adherence to such practices may lead to significant delays in clinical trials or in obtaining regulatory approval of product candidates or the ultimate launch of products based on our product candidates into the market. Failure by our current or future third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant pre-market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions, and criminal prosecutions. If the safety of any product supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical studies, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or impair our reputation.

***We will need to continue to manage our organization and we may encounter difficulties with our staffing and any future transitions, which could adversely affect our results of operations.***

We will need to manage our operations and facilities effectively in order to advance our drug development programs (including ITI-007 and ITI-214), facilitate any future collaborations, and pursue other development activities. It is possible that our infrastructure may be inadequate to support our future efforts and growth. In particular, we may have to develop internal sales, marketing, and distribution capabilities if we decide to market any drug that we may successfully develop. We may not successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals.

***Our ability to generate product revenues will be diminished if our products do not receive coverage from payors or sell for inadequate prices, or if patients are unable to obtain adequate levels of reimbursement.***

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and reimbursement from governmental health care programs, such as Medicare and Medicaid, and commercial payors is critical to new product

acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are

## Table of Contents

already available or subsequently become available. Even if we obtain coverage for any approved products, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use any products we may market unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of those products.

In addition, the market for any products for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Third-party payors, whether foreign or domestic, governmental or commercial, are developing increasingly sophisticated methods of controlling health care costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage will be obtained. If we are unable to obtain coverage of, and adequate payment levels for, our products from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize any approved products and thereby adversely impact our profitability, results of operations, financial condition, and future success.

***In the future, if we have products that are approved, health care legislation may make it more difficult to receive revenues from those products.***

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals in recent years to change the health care system in ways that could impact our ability to sell our products profitably. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, ACA, became law in the United States. The ACA substantially changed the way health care is financed by both governmental and private insurers and significantly affects the health care industry. Among the provisions of ACA of importance to our potential product candidates are the following:

imposition of an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government health care programs;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively;

expansion of health care fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

expansion of eligibility criteria for Medicaid programs;

**Table of Contents**

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting any payments or transfers of value made or distributed to prescribers, teaching hospitals and other health care providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year;

a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Many of the details regarding the implementation of the ACA are yet to be determined and, at this time, it remains unclear what the full effect that the ACA will have on our business. At this time, it remains unclear whether there will be any further changes made to the ACA, whether in part or in its entirety.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with any products we may market, which could negatively impact our profitability.

We expect that the ACA, as well as other health care reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other health care reforms may prevent us from being able to generate revenue, attain profitability, or commercialize any products for which we receive regulatory approval.

***If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any products we may develop, we may not be able to generate product revenue.***

We do not currently have an organization for the sales, marketing or distribution of pharmaceutical products. In order to market any products that may be approved by the FDA, we must build our sales, marketing, managerial, and related capabilities or make arrangements with third parties to perform these critical commercial services. There are risks involved with both establishing our own sales, marketing, managerial and related capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we

would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We also may not be successful entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our

## **Table of Contents**

products effectively, which could damage our reputation. If we do not establish adequate sales, marketing, and distribution capabilities, whether independently or in collaboration with third parties, we will not be successful in commercializing our product candidates, may not be able to generate product revenue and may not become profitable.

### ***There are possible limitations on our use of net operating losses.***

As of December 31, 2015, we had net operating loss carryforwards of approximately \$174.8 million to reduce any future federal and state taxable income through 2035. Since we had net operating loss carryforwards as of December 31, 2015, 2014 and 2013, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations. The net operating loss carryforwards of approximately \$174.8 million as of December 31, 2015 will begin to expire in the year 2030 if unused. The use of our net operating loss carryforwards may be restricted due to changes in our ownership, including as a result of our public offerings in March 2015 and September 2015.

Under Section 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, substantial changes in our ownership may limit the amount of net operating loss carryforwards, or NOLs, and tax credit carryforwards that could be utilized annually in the future to offset taxable income.

For the year ended December 31, 2015 we performed a Section 382 ownership analysis and determined that an ownership change occurred (within the meaning of Section 382 of the Code) in 2015. Based on the analysis performed, however, we do not believe that the Section 382 annual limitation will impact our ability to utilize the tax attributes that existed as of the date of the ownership change in a material manner. If we experience an ownership change in the future, the tax benefits related to the NOLs and tax credit carryforwards may be further limited or lost.

### ***Security breaches, loss of data and other disruptions could compromise sensitive information related to our business, prevent us from accessing critical information or expose us to liability, which could adversely affect our business and our reputation.***

In the ordinary course of our business, we, our clinical research organizations and other third parties on which we rely collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems. These applications and data encompass a wide variety of business critical information including research and development information and business and financial information.

The secure processing, storage, maintenance and transmission of this critical information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure may be vulnerable to attacks by hackers, viruses, breaches, interruptions due to employee error, malfeasance or other disruptions, lapses in compliance with privacy and security mandates, or damage from natural disasters, terrorism, war and telecommunication and electrical failures. Any such event could compromise our networks and the information stored there could be accessed by unauthorized parties, publicly disclosed, lost or stolen. We have measures in place that are designed to detect and respond to such security incidents and breaches of privacy and security mandates. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as the Health Insurance Portability and Accountability Act of 1996, government enforcement actions and regulatory penalties. Unauthorized access, loss or dissemination could also disrupt our operations, including our ability to conduct research and development activities, process and prepare company financial information, manage various general and administrative aspects of our business and damage our reputation, any of which could adversely affect our business. For example, the loss of clinical trial data from

completed or

42



**Table of Contents**

ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, there can be no assurance that we will promptly detect any such disruption or security breach, if at all. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

**Risks Related to Our Intellectual Property**

***Our ability to compete may be undermined if we do not adequately protect our proprietary rights.***

Our commercial success depends on obtaining and maintaining proprietary rights to our product candidates and technologies and their uses, as well as successfully defending these rights against third-party challenges. We will only be able to protect our product candidates, proprietary technologies, and their uses from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. We have patent rights under issued patents in many cases covering our ITI-007 and ITI-002 development programs. Nonetheless, the issued patents and patent applications covering our primary technology programs remain subject to uncertainty and continuous monitoring and action by us due to a number of factors, including:

we may not have been the first to make the inventions covered by our pending patent applications or issued patents;

we may not have been the first to file patent applications for our product candidates or the technologies we rely upon;

others may independently develop similar or alternative technologies or duplicate any of our technologies;

our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;

any or all of our pending patent applications may not result in issued patents;

we may not seek or obtain patent protection in all countries that will eventually provide a significant business opportunity;

any patents issued to us or our collaborators may not provide a basis for commercially viable products, may not provide us with any competitive advantages or may be challenged by third parties;

our proprietary technologies may not be patentable;

others may design around our patent claims to produce competitive products which fall outside of the scope of our patents;

others may identify prior art which could invalidate our patents; and

changes to patent laws may limit the exclusivity rights of patent holders.

Even if we have or obtain patents covering our product candidates or technologies, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights of others. Others have or may have filed, and in the future are likely to file, patent applications covering compounds, assays, genes, gene products and therapeutic products that are similar or identical to ours. There are many issued U.S. and foreign patents relating to genes, nucleic acids, polypeptides, chemical compounds or therapeutic products, and some of these may encompass reagents utilized in the identification of candidate drug compounds or compounds that we desire to commercialize. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the area of central nervous system disorders and the other fields in which we are developing products. These could materially affect our ability to develop our product candidates or sell our products. Because patent applications can take many years to issue, there may be currently pending

## **Table of Contents**

applications, unknown to us, that may later result in issued patents that our product candidates or technologies may infringe. These patent applications may have priority over patent applications filed by us.

We regularly conduct searches to identify patents or patent applications that may prevent us from obtaining patent protection for our proprietary compounds or that could limit the rights we have claimed in our patents and patent applications. Disputes may arise regarding the ownership or inventorship of our inventions. It is difficult to determine how such disputes would be resolved. Others may challenge the validity of our patents. If our patents are found to be invalid, we will lose the ability to exclude others from making, using or selling the inventions claimed in our patents.

Some of our academic institutional licensors, research collaborators and scientific advisors have rights to publish data and information to which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information will be impaired. Additionally, any employee whose employment with us terminates, whether voluntarily by the employee or by us in connection with restructurings or otherwise, may seek future employment with our competitors. Although each of our employees is required to sign a confidentiality agreement with us at the time of hire, we cannot guarantee that the confidential nature of our proprietary information will be maintained in the course of such future employment. In addition, technology that we may license-in may become important to some aspects of our business. We generally will not control the patent prosecution, maintenance or enforcement of in-licensed technology.

***Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.***

Because we operate in the highly technical field of drug discovery and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. We enter into confidentiality and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties any confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. The failure to obtain or maintain trade secret protection could adversely affect our competitive position.

***A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business.***

There is significant litigation in our industry regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. If our drug development activities are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. We may need to resort to litigation to enforce a patent issued to us, protect our trade secrets or determine the scope and validity of third-party proprietary rights. From time to time, we may hire scientific personnel formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject

to allegations of trade secret misappropriation or other similar claims as a result of their prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We also may not be able to afford the costs of litigation.

---

**Table of Contents**

***The patent applications of pharmaceutical and biotechnology companies involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.***

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. The U.S. Patent and Trademark Office's, or USPTO's, standards are uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings in the USPTO (and foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office), which proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. Similarly, opposition or invalidity proceedings could result in loss of rights or reduction in the scope of one or more claims of a patent in foreign jurisdictions. In addition, such interference, reexamination and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

In addition, changes in or different interpretations of patent laws in the United States and foreign countries may permit others to use our discoveries or to develop and commercialize our technology and products without providing any compensation to us or may limit the number of patents or claims we can obtain. In particular, there have been proposals to shorten the exclusivity periods available under U.S. patent law that, if adopted, could substantially harm our business. The product candidates that we are developing are protected by intellectual property rights, including patents and patent applications. If any of our product candidates becomes a marketable product, we will rely on our exclusivity under patents to sell the compound and recoup our investments in the research and development of the compound. If the exclusivity period for patents is shortened, then our ability to generate revenues without competition will be reduced and our business could be materially adversely impacted. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans and, in these countries, patent protection may not be available at all to protect our product candidates. In addition, U.S. patent laws may change, which could prevent or limit us from filing patent applications or patent claims to protect our products and/or technologies or limit the exclusivity periods that are available to patent holders. For example, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was recently signed into law and includes a number of significant changes to U.S. patent law. These include changes to transition from a first-to-invent system to a first-to-file system and to the way issued patents are challenged. These changes may favor larger and more established companies that have more resources to devote to patent application filing and prosecution. The USPTO has been in the process of implementing regulations and procedures to administer the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act may affect our ability to obtain, enforce or defend our patents. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will ultimately have on the cost of prosecuting our patent applications, our ability to obtain patents based on our discoveries and our ability to enforce or defend our issued patents.

If we fail to obtain and maintain patent protection and trade secret protection of our product candidates, proprietary technologies and their uses, we could lose our competitive advantage and competition we face would increase, reducing our potential revenues and adversely affecting our ability to attain or maintain profitability.

### **Risks Related to Our Industry**

***We will be subject to stringent regulation in connection with the marketing of any products derived from our product candidates, which could delay the development and commercialization of our products.***

The pharmaceutical industry is subject to stringent regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Neither we nor our collaborators can market a pharmaceutical product in the United States until it has completed rigorous preclinical testing and clinical trials

## Table of Contents

and an extensive regulatory clearance process implemented by the FDA. Satisfaction of regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product, and requires substantial resources. Even if regulatory approval is obtained, it may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, and/or marketing of such products, and requirements for post-approval studies, including additional research and development and clinical trials. These limitations may limit the size of the market for the product or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues and continue our business.

Outside the United States, the ability to market a product is contingent upon receiving approval from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing, and reimbursement vary widely from country to country. Only after the appropriate regulatory authority is satisfied that adequate evidence of safety, quality, and efficacy has been presented will it grant a marketing authorization. Approval by the FDA does not automatically lead to the approval by regulatory authorities outside the United States and, similarly, approval by regulatory authorities outside the United States will not automatically lead to FDA approval.

***Many of our competitors have greater resources and capital than us, putting us at a competitive disadvantage. If our competitors develop and market products that are more effective than our product candidates, they may reduce or eliminate our commercial opportunity.***

Competition in the pharmaceutical and biotechnology industries is intense and increasing. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the United States and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our drug development programs.

For example, our potential products for the treatment of schizophrenia would compete with, among other branded products, Abilify<sup>®</sup>, marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical, Fanapt<sup>®</sup>, marketed by Novartis Pharmaceuticals, Seroquel XR<sup>®</sup>, marketed by AstraZeneca, Invega<sup>®</sup>, marketed by Janssen, VRAYLAR<sup>®</sup>, marketed by Allergan, Rexulti<sup>®</sup> marketed by Otsuka Pharmaceutical and Latuda<sup>®</sup>, marketed by Sunovion. In addition, our product candidates, if approved, will compete with, among other generic antipsychotic drugs, haloperidol, risperidone, quetiapine, olanzapine and clozapine.

Many of our competitors and their collaborators have significantly greater experience than we do in the following:

identifying and validating targets;

screening compounds against targets;

preclinical studies and clinical trials of potential pharmaceutical products; and

obtaining FDA and other regulatory approvals.

In addition, many of our competitors and their collaborators have substantially greater capital and research and development resources, manufacturing, sales and marketing capabilities, and production facilities. Smaller companies

also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate drug targets and to discover novel small molecule drugs. Our competitors, either alone or with their collaborators, may succeed in developing drugs that are more effective, safer, more affordable, or more easily administered than ours and may achieve patent protection or



## **Table of Contents**

commercialize drugs sooner than us. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Our failure to compete effectively could have a material adverse effect on our business.

***Any claims relating to improper handling, storage, or disposal of biological, hazardous, and radioactive materials used in our business could be costly and delay our research and development efforts.***

Our research and development activities involve the controlled use of potentially harmful hazardous materials, including volatile solvents, biological materials such as blood from patients that have the potential to transmit disease, chemicals that cause cancer, and various radioactive compounds. Our operations also produce hazardous waste products. We face the risk of contamination or injury from the use, storage, handling or disposal of these materials. We are subject to federal, state and local laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. The cost of compliance with these laws and regulations could be significant, and current or future environmental regulations may impair our research, development, or production efforts. If one of our employees were accidentally injured from the use, storage, handling, or disposal of these materials, the medical costs related to his or her treatment would be covered by our workers' compensation insurance policy. However, we do not carry specific biological or hazardous waste insurance coverage and our general liability insurance policy specifically excludes coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be subject to criminal sanctions or fines or be held liable for damages, our operating licenses could be revoked, and we could be required to suspend or modify our operations and our research and development efforts.

***Consumers may sue us for product liability, which could result in substantial liabilities that exceed our available resources and damage our reputation.***

Researching, developing, and commercializing drug products entail significant product liability risks. Liability claims may arise from our and our collaborators' use of products in clinical trials and the commercial sale of those products. Consumers may make these claims directly and our collaborators or others selling these products may seek contribution from us if they receive claims from consumers. We have obtained limited product liability insurance coverage for our clinical trials. Our product liability insurance coverage for clinical trials is currently limited to an aggregate of \$30 million. As such, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Although we currently have product liability insurance that covers our clinical trials, we will need to increase and expand this coverage as we commence larger scale trials and if our product candidates are approved for commercial sale. This insurance may be prohibitively expensive or may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products that we or our collaborators develop. Product liability claims could have a material adverse effect on our business and results of operations. Our liability could exceed our total assets if we do not prevail in a lawsuit from any injury caused by our drug products.

## **Risks Related to Owning Our Common Stock**

***Numerous factors could result in substantial volatility in the trading price of our stock.***

During the year ended December 31, 2015, the price per share of our common stock on the NASDAQ Global Select Market has ranged from a high of \$60.79 to a low of \$16.29. We have several stockholders, including affiliated stockholders, who hold substantial blocks of our stock. Sales of large numbers of shares by any of our large stockholders could adversely affect our trading price. If stockholders holding shares of our common stock sell,

indicate an intention to sell, or if it is perceived that they will sell, substantial amounts of their common stock in the public market, the trading price of our common stock could decline.

**Table of Contents**

In addition, the trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

timing and announcement of regulatory developments and approvals or preliminary, interim or final results of clinical trials;

actual or anticipated quarterly variation in our results of operations or the results of our competitors;

announcements of medical innovations or new products by our competitors;

issuance of new or changed securities analysts' reports or recommendations for our stock;

developments or disputes concerning our intellectual property or other proprietary rights;

commencement of, or our involvement in, litigation;

market conditions in the biopharmaceutical industry;

any future sales of our common stock or other securities in connection with raising additional capital or otherwise;

any major change to the composition of our board of directors or management; and

general economic conditions and slow or negative growth of our markets.

The stock market in general, and market prices for the securities of biotechnology companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance. In several recent situations where the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

***Raising additional capital may cause dilution to existing stockholders, restrict our operations or require us to relinquish rights.***

We will need to satisfy our future cash needs through public or private sales of our equity securities, sales of debt securities, the incurrence of debt from commercial lenders, strategic collaborations, licensing a portion or all of our

product candidates and technology and, to a lesser extent, grant funding. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or grant licenses on terms that are not favorable to us.

***The price of our common stock could be subject to volatility related or unrelated to our operations.***

The market price of our common stock could fluctuate substantially due to a variety of factors, including market perception of our ability to meet our growth projections and expectations, quarterly operating results of other companies in the same industry, trading volume in our common stock, changes in general conditions in the economy and the financial markets or other developments affecting our business and the business of others in our industry. In addition, the stock market itself is subject to extreme price and volume fluctuations. This volatility has had a significant effect on the market price of securities issued by many companies for reasons related and unrelated to their operating performance and could have the same effect on our common stock.

**Table of Contents**

***We will incur increased costs and demands upon management as a result of complying with the laws and regulations affecting public companies, which could harm our operating results.***

As a public company, we have incurred and will incur significant legal, accounting and other expenses, including costs associated with public company reporting requirements. We also have incurred and will incur costs associated with current corporate governance requirements, including requirements under Section 404 and other provisions of the Sarbanes-Oxley Act, as well as rules implemented by the SEC or the NASDAQ Global Select Market or any other stock exchange or inter-dealer quotations system on which our common stock may be listed in the future. The expenses incurred by public companies for reporting and corporate governance purposes have increased dramatically in recent years.

***If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.***

We are required to comply with Section 404 of the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to maintain effective internal control over financial reporting. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting. In addition, we are required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting beginning with this annual report on Form 10-K for the fiscal year ended December 31, 2015. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. We currently do not have an internal audit group, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we fail to maintain the effectiveness of our internal controls or fail to comply in a timely manner with the requirements of the Sarbanes-Oxley Act, or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, this could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources. In addition, if our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Our ability to successfully implement our business plan and comply with Section 404 requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and to obtain an unqualified report on internal controls from our independent registered public accounting firm as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our common stock, and could adversely affect our ability to access the capital markets.

***We are no longer an emerging growth company and are not able to take advantage of the reduced disclosure requirements applicable to emerging growth companies.***

We were an emerging growth company under the Jumpstart Our Business Startups Act, or JOBS Act, until December 31, 2015. As an emerging growth company, we took advantage of certain exemptions from various reporting requirements that are applicable to other public companies. On December 31, 2015, we became a large

## **Table of Contents**

accelerated filer and the reduced disclosure obligations of emerging growth companies are no longer available to us. As a result, we will need to comply with the independent auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act beginning with this annual report on Form 10-K for the year ended December 31, 2015, will be required to hold a say-on-pay vote and a say-on-frequency vote at our 2016 annual meeting of stockholders, and will no longer be entitled to provide the reduced executive compensation disclosures permitted by emerging growth companies beginning with this annual report on Form 10-K for the year ended December 31, 2015 and the proxy statement for our 2016 annual meeting of stockholders. We expect that our transition from emerging growth company to large accelerated filer will require additional attention from management and will result in increased costs to us, which could include higher legal fees, accounting and related fees and fees associated with investor relations activities, among others.

***If securities or industry analysts do not publish, or cease publishing, research or reports about us, our business or our market, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.***

The trading market for our common stock is and will be influenced by whether industry or securities analysts publish or continue to publish research and reports about us, our business, our market or our competitors and, to the extent analysts do publish such reports, what they publish in those reports. We may not continue to have or to obtain analyst coverage in the future. Any analysts that do cover us may make adverse recommendations regarding our stock, adversely change their recommendations from time to time, and/or provide more favorable relative recommendations about our competitors. If any analyst who covers us or may cover us in the future were to cease coverage of our company or fail to regularly publish reports on us, or if analysts fail to cover us or publish reports about us at all, we could lose, or never gain, visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

***Provisions of the Delaware law, our restated certificate of incorporation and our restated bylaws may delay or prevent a takeover which may not be in the best interests of our stockholders.***

The provisions of Delaware law and our restated certificate of incorporation and restated bylaws could discourage or make it more difficult to accomplish a proxy contest or other change in our management or the acquisition of control by a holder of a substantial amount of our voting stock. It is possible that these provisions could make it more difficult to accomplish, or could deter, transactions that stockholders may otherwise consider to be in their best interests or in our best interests. These provisions are intended to enhance the likelihood of continuity and stability in the composition of our board of directors and in the policies formulated by the board of directors and to discourage certain types of transactions that may involve an actual or threatened change of our control. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy fights. Such provisions also may have the effect of preventing changes in our management.

***We do not anticipate paying cash dividends in the foreseeable future.***

We currently intend to retain any future earnings for funding growth. We do not anticipate paying any dividends in the foreseeable future. As a result, you should not rely on an investment in our securities if you require dividend income. Capital appreciation, if any, of our shares may be your sole source of gain for the foreseeable future. Moreover, you may not be able to re-sell your shares at or above the price you paid for them.

## **CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS**

This report includes forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity,



**Table of Contents**

performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Words such as, but not limited to, believe, expect, anticipate, estimate, intend, may, plan, potential, predict, project, targets, likely, will, continue, and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this report, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. The description of our Business set forth in Item 1, the Risk Factors set forth in this Item 1A and our Management's Discussion and Analysis of Financial Condition and Results of Operations set forth in Item 7 as well as other sections in this report, discuss some of the factors that could contribute to these differences. These forward-looking statements include, among other things, statements about:

the accuracy of our estimates regarding expenses, future revenues, uses of cash, capital requirements and the need for additional financing;

the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials;

the timing of and our ability to obtain and maintain regulatory approval of our existing product candidates, any product candidates that we may develop, and any related restrictions, limitations, and/or warnings in the label of any approved product candidates;

our plans to research, develop and commercialize our current and future product candidates;

our collaborators' election to pursue research, development and commercialization activities;

our ability to obtain future reimbursement and/or milestone payments from our collaborators;

our ability to attract collaborators with development, regulatory and commercialization expertise;

our ability to obtain and maintain intellectual property protection for our product candidates;

our ability to successfully commercialize our product candidates;

the size and growth of the markets for our product candidates and our ability to serve those markets;

the rate and degree of market acceptance of any future products;

the success of competing drugs that are or become available;

regulatory developments in the United States and other countries;

the performance of our third-party suppliers and manufacturers and our ability to obtain alternative sources of raw materials;

our ability to obtain additional financing;

our use of the proceeds from our securities offerings;

any restrictions on our ability to use our net operating loss carryforwards;

our exposure to investment risk, interest rate risk and capital market risk;

our expectations regarding the additional management attention and costs that will be required as we transition from an emerging growth company to a large accelerated filer; and

our ability to attract and retain key scientific or management personnel.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements

**Table of Contents**

we make. We have included important cautionary statements in this report, particularly in the Risk Factors set forth in Item 1A of this Annual Report on Form 10-K, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this report and the documents that we reference in this report and have filed as exhibits to this report completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this report are made as of the date of this report, and we do not assume, and specifically disclaim, any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

**Item 1B. UNRESOLVED STAFF COMMENTS**

None.

**Item 2. PROPERTIES**

Our headquarters are located at 430 East 29th Street, New York, New York 10016, where we occupy approximately 16,753 square feet of useable office and laboratory space. The term of the lease, as amended, expires January 31, 2027. We also lease office space in Towson, Maryland on a month to month basis.

**Item 3. LEGAL PROCEEDINGS**

We are not currently a party to any material legal proceedings.

**Item 4. MINE SAFETY DISCLOSURES**

Not applicable.

**Table of Contents****PART II****Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES****Market Information**

From December 20, 2013 through January 30, 2014, our common stock was quoted on the OTC Markets OTCQB tier, or OTCQB, under the symbol ITCI. On January 31, 2014, our common stock commenced trading on the NASDAQ Global Select Market under the symbol ITCI and ceased being quoted on the OTCQB. The high and low bid quotations per share of our common stock as reported by the OTCQB and the high and low sales prices per share of our common stock as reported by NASDAQ for the applicable periods when the common stock was quoted on the OTCBB or listed on the NASDAQ Global Select Market, as applicable, since the common stock commenced public trading are set forth below:

<b>Year Ended December 31, 2015</b>	<b>High</b>	<b>Low</b>
First Quarter	\$ 30.72	\$ 16.29
Second Quarter	\$ 35.45	\$ 19.86
Third Quarter	\$ 60.79	\$ 21.19
Fourth Quarter	\$ 59.96	\$ 37.75

<b>Year Ended December 31, 2014</b>	<b>High</b>	<b>Low</b>
First Quarter	\$ 21.26	\$ 10.00
Second Quarter	\$ 19.60	\$ 14.53
Third Quarter	\$ 19.77	\$ 12.67
Fourth Quarter	\$ 19.00	\$ 13.37

**Stockholders**

As of February 25, 2016, we had 43,202,709 outstanding shares of common stock and no outstanding shares of preferred stock. As of February 25, 2016, there were approximately 125 holders of record of our outstanding shares of common stock.

**Dividends**

We have never paid cash dividends on any of our capital stock and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

**Unregistered Sales of Securities**

Not applicable.

**Issuer Purchases of Equity Securities**

Not applicable.

**Use of Proceeds from Registered Securities**

On February 5, 2014, we completed our initial public offering of 7,063,300 shares of our common stock at a price of \$17.50 per share for aggregate gross proceeds of approximately \$123.6 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1, which was declared effective on January 30, 2014 (File No. 333-193313), and a registration statement on Form S-1 filed pursuant to Rule 462(b) promulgated under the Securities Act (File No. 333-193676). Leerink

**Table of Contents**

Partners LLC and Cowen and Company, LLC acted as joint book-running managers for the offering and as representatives of the underwriters. Guggenheim Securities, LLC and JMP Securities LLC acted as co-managers for the offering. The offering commenced on January 24, 2014 and did not terminate until the sale of all of the shares offered.

We received aggregate net proceeds from the offering of approximately \$115.4 million, after deducting approximately \$7.4 million of underwriting discounts and commissions, and approximately \$0.8 million of offering expenses payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to our directors or officers or their associates or to persons owning 10 percent or more of our common stock or to any of our affiliates.

As of December 31, 2015, we have used the net proceeds of the offering primarily for working capital purposes, including recurring expenses and preclinical and clinical trial costs related to the development of ITI-007.

**Table of Contents****Item 6. SELECTED FINANCIAL DATA**

The following table sets forth consolidated financial data with respect to the Company for each of the five years in the period ended December 31, 2015. The selected financial data for each of the five years in the period ended December 31, 2015 have been derived from our audited consolidated financial statements. The consolidated balance sheets as of December 31, 2015 and 2014 and the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2015, and the report thereon, are included elsewhere in this Annual Report on Form 10-K. The information below should be read in conjunction with the consolidated financial statements (and notes thereon) and Management's Discussion and Analysis of Financial Condition and Results of Operations, included in Item 7.

	2015	2014	2013	2012	2011
<b>Statements of Operations:</b>					
Revenues:					
License and collaboration revenue	\$ 30,659	\$ 547,546	\$ 2,737,002	\$ 3,117,991	\$ 22,327,464
Grant revenue	60,705	29,755			1,034,495
<b>Total Revenues</b>	<b>91,364</b>	<b>577,301</b>	<b>2,737,002</b>	<b>3,117,991</b>	<b>23,361,959</b>
Costs and expenses:					
Research and development	87,718,074	21,226,345	23,027,578	15,486,476	7,654,546
General and administrative	18,187,286	10,337,679	5,976,276	4,034,925	4,612,450
<b>Total costs and expenses</b>	<b>105,905,360</b>	<b>31,564,024</b>	<b>29,003,854</b>	<b>19,521,401</b>	<b>12,266,996</b>
(Loss) Income from operations	(105,813,996)	(30,698,223)	(26,266,852)	(16,403,410)	11,094,963
Interest expense		(7,073)	(612,963)	(193,498)	(15)
Interest income	1,022,455	303,936	29,617	39,002	62,315
Income taxes	(1,600)	(1,600)	(18,000)	(32,921)	(64,834)
<b>Net (Loss) Income</b>	<b>\$ (104,793,141)</b>	<b>\$ (30,691,460)</b>	<b>\$ (26,868,198)</b>	<b>\$ (16,590,827)</b>	<b>\$ 11,092,429</b>
Net (Loss) Income per common share:					
Basic	\$ (2.91)	\$ (1.07)	\$ (1.56)	\$ (2.96)	\$ 1.98
Diluted	\$ (2.91)	\$ (1.07)	\$ (1.56)	\$ (2.96)	\$ 1.47
Weighted average number of common shares:					
Basic	36,069,237	28,650,067	17,260,768	5,607,539	5,601,495
Diluted	36,069,237	28,650,067	17,260,768	5,607,539	7,558,150
			<b>December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>	<b>2012</b>	<b>2011</b>
<b>Balance Sheet data:</b>					
Cash and cash equivalents	\$ 47,159,303	\$ 61,325,044	\$ 35,150,924	\$ 15,645,528	\$ 13,693,215
Total assets	484,103,528	131,111,769	38,449,312	19,823,680	23,594,725
Total liabilities	7,860,617	10,557,064	6,834,037	2,839,595	5,702,422
Accumulated deficit	(193,049,098)	(88,255,957)	(57,564,497)	(30,696,299)	(14,105,472)

Total stockholders equity	476,242,911	120,554,705	31,615,275	16,984,085	17,892,303
---------------------------	-------------	-------------	------------	------------	------------



---

**Table of Contents****Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

*The following discussion of the financial condition and results of our operations and our wholly-owned subsidiary should be read in conjunction with the financial statements and the notes to those statements appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should read the Risk Factors set forth in Item 1A of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

**Overview**

We are a biopharmaceutical company focused on the discovery and clinical development of innovative, small molecule drugs that address underserved medical needs in neuropsychiatric and neurological disorders by targeting intracellular signaling mechanisms within the central nervous system, or CNS. ITI-007 is our lead drug development candidate with mechanisms of action that, we believe, may represent an effective treatment across multiple therapeutic indications. In our pre-clinical and clinical trials to date, ITI-007 combines potent serotonin 5-HT<sub>2A</sub> receptor antagonism, dopamine receptor phosphoprotein modulation, or DPPM, glutamatergic modulation, and serotonin reuptake inhibition into a single drug candidate for the treatment of acute and residual schizophrenia and for the treatment of bipolar disorder, including bipolar depression. At dopamine D<sub>2</sub> receptors, ITI-007 has been demonstrated to have dual properties and to act as both a pre-synaptic partial agonist and a post-synaptic antagonist. ITI-007 has also been demonstrated to have affinity for dopamine D<sub>1</sub> receptors and indirectly stimulate phosphorylation of glutamatergic NMDA GluN<sub>2B</sub> receptors in a mesolimbic specific manner. We believe that this regional selectivity in brain areas thought to mediate the efficacy of antipsychotic drugs, together with serotonergic, glutamatergic, and dopaminergic interactions, may result in efficacy for a broad array of symptoms associated with schizophrenia and bipolar disorder with improved psychosocial function. The serotonin reuptake inhibition potentially allows for antidepressant activity in the treatment of schizoaffective disorder, other disorders with co-morbid depression, and/or as a stand-alone treatment for major depressive disorder. We believe ITI-007 may also be useful for the treatment of other psychiatric and neurodegenerative disorders, particularly behavioral disturbances associated with dementia, autism, and other CNS diseases. ITI-007 is in Phase 3 clinical development as a novel treatment for schizophrenia and bipolar depression.

*ITI-007 for the Treatment of Schizophrenia*

In September 2015, we announced top-line clinical results from our first Phase 3 clinical trial of ITI-007 for the treatment of patients with schizophrenia. This randomized, double-blind, placebo-controlled Phase 3 clinical trial was conducted at 12 sites in the United States with 450 patients randomized (1:1:1) to receive either 60 mg of ITI-007, 40 mg of ITI-007 or placebo once daily in the morning for 28 days. The pre-specified primary efficacy measure was change from baseline versus placebo at study endpoint (4 weeks) on the centrally rated Positive and Negative Syndrome Scale, or PANSS, total score. In this trial, the once-daily dose of 60 mg of ITI-007 met the primary endpoint and demonstrated antipsychotic efficacy with statistically significant superiority over placebo at week 4 (study endpoint) with additional improvements observed in social function. Moreover, the 60 mg dose of ITI-007 showed significant antipsychotic efficacy as early as week 1, which was maintained at every time point throughout the entire study. ITI-007 showed a dose-related improvement in symptoms of schizophrenia with the 40 mg dose approximating the trajectory of improvement seen with the 60 mg dose, but the effect with 40 mg did not reach statistical significance on the primary endpoint. In addition, the 60 mg dose of ITI-007 met the key secondary endpoint of statistically significant improvement on the Clinical Global Impression Scale for Severity of Illness, or

CGI-S. The 40 mg dose of ITI-007 also demonstrated a statistically significant improvement versus placebo on the CGI-S, though not formally tested against placebo as a key

---

**Table of Contents**

secondary endpoint since it did not separate on the primary endpoint. Consistent with previous studies, ITI-007 had a favorable safety and tolerability profile as evidenced by motoric, metabolic, and cardiovascular characteristics similar to placebo, and no clinically significant changes in akathisia, extrapyramidal symptoms, prolactin, body weight, glucose, insulin, or lipids.

In September 2015, we also announced top-line data from an open-label positron emission tomography, or PET, study of ITI-007 examining brain occupancy of striatal D<sub>2</sub> receptors. This study was conducted in patients diagnosed with schizophrenia who were otherwise healthy and stable with respect to their psychosis. After washout from their previous antipsychotic medication for at least two weeks, PET was used to determine target occupancy in brain regions at baseline (drug-free) and again after two weeks of once daily ITI-007 oral administration. In this trial, the 60 mg dose of ITI-007 was associated with a mean of approximately 40% striatal dopamine D<sub>2</sub> receptor occupancy. As predicted by preclinical and earlier clinical data, ITI-007 demonstrated antipsychotic effect at relatively low striatal D<sub>2</sub> receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D<sub>2</sub> receptors. We believe this mechanism likely contributes to the favorable safety profile of ITI-007, with reduced risk for hyperprolactinemia, akathisia, extrapyramidal symptoms, and other motoric side effects.

The top-line results from our first Phase 3 clinical trial of ITI-007 confirm the earlier Phase 2 results that we announced in December 2013, in which ITI-007 exhibited antipsychotic efficacy in a randomized, double-blind, placebo and active controlled clinical trial in patients with an acutely exacerbated episode of schizophrenia. In this Phase 2 trial, 335 patients were randomized to receive one of four treatments: 60 mg of ITI-007, 120 mg of ITI-007, 4 mg of risperidone (active control) or placebo in a 1:1:1:1 ratio, orally once daily for 28 days. The primary endpoint for this clinical trial was change from baseline to Day 28 on the PANSS total score. In this study, ITI-007 met the trial's pre-specified primary endpoint, improving symptoms associated with schizophrenia as measured by a statistically significant and clinically meaningful decrease in the PANSS total score. The trial also met key secondary outcome measures related to efficacy on PANSS subscales and safety. We are also conducting a second Phase 3 clinical trial in schizophrenia that we initiated in the second quarter of 2015, with over 600 patients planned to be enrolled in the trial. In this trial, we are randomizing patients to two doses of ITI-007 (60 mg or 20 mg), risperidone (active control) or placebo over a 6-week treatment duration, and the primary outcome measure is change from baseline to Day 42 on the PANSS total score. We expect patient enrollment will be completed in the second quarter of 2016. Subject to timely enrollment, we anticipate top-line results from the second Phase 3 clinical trial will be available in mid-2016.

In addition to our two Phase 3 clinical trials, we will need to complete other clinical and non-clinical trials and manufacturing and pre-commercialization activities necessary to support the submission of a planned NDA for ITI-007 in schizophrenia, which we currently expect could occur in the first half of 2017.

*ITI-007 for the Treatment of Depressive Episodes Associated with Bipolar Disorder (Bipolar Depression)*

Our bipolar depression program consists of two Phase 3 multi-center, randomized, double-blind, placebo-controlled clinical trials: one to evaluate ITI-007 as a monotherapy and the other to evaluate ITI-007 as an adjunctive therapy with lithium or valproate. In each trial, approximately 550 patients with a clinical diagnosis of Bipolar I or Bipolar II disorder and who are experiencing a current major depressive episode will be randomized to receive one of three treatments: 60 mg ITI-007, 40 mg ITI-007, or placebo in a 1:1:1 ratio orally once daily for 6 weeks. In the ITI-007-401 trial, patients will receive ITI-007 or placebo as a monotherapy. In the ITI-007-402 trial, patients will receive ITI-007 or placebo adjunctive to their existing mood stabilizer lithium or valproate. We initiated our bipolar depression program in the third quarter of 2015.

The primary endpoint for both clinical trials is change from baseline at Day 42 on the Montgomery-Åsberg Depression Rating Scale, or MADRS, total score versus placebo. The MADRS is a well-validated 10-item checklist that measures the ability of a drug to reduce overall severity of depressive symptoms. Individual items

---

**Table of Contents**

are rated by an expert clinician on a scale of 0 to 6 in which a score of 6 represents the most depressed evaluation for each item assessed. The total score ranges from 0 to 60. Secondary endpoints include measures of social function and quality of life that may illustrate the differentiated clinical profile of ITI-007. Safety and tolerability are also assessed in both clinical trials.

*Other Indications for ITI-007*

In the fourth quarter of 2014, we announced the top-line data from ITI-007-200, a Phase 1/2 clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of ITI-007 in healthy geriatric subjects and in patients with dementia, including Alzheimer's disease. The completion of this study marks an important milestone in our strategy to develop low doses of ITI-007 for the treatment of behavioral disturbances associated with dementia and related disorders. The ITI-007-200 trial results to date indicate that ITI-007 is safe and well-tolerated across a range of low doses, has linear- and dose-related pharmacokinetics and improves cognition in the elderly. The most frequent adverse event was mild sedation at the higher doses. We believe these results further position ITI-007 as a development candidate for the treatment of behavioral disturbances in patients with dementia and other neuropsychiatric and neurological conditions. We plan to initiate additional late phase clinical programs evaluating ITI-007 in patients with behavioral disturbances associated with dementia and related disorders, including Alzheimer's disease, in the first half of 2016.

We are also pursuing clinical development of ITI-007 for the treatment of additional CNS diseases and disorders. At the lowest doses, ITI-007 has been demonstrated to act primarily as a potent 5-HT<sub>2A</sub> serotonin receptor antagonist. As the dose is increased, additional benefits are derived from the engagement of additional drug targets, including modest dopamine receptor modulation and modest inhibition of serotonin transporters. We believe that combined interactions at these receptors may provide additional benefits above and beyond selective 5-HT<sub>2A</sub> antagonism for treating agitation, aggression and sleep disturbances in diseases that include dementia, Alzheimer's disease, Huntington's disease and autism spectrum disorders, while avoiding many of the side effects associated with more robust dopamine receptor antagonism. As the dose of ITI-007 is further increased, leading to moderate dopamine receptor modulation, inhibition of serotonin transporters, and indirect glutamate modulation, these actions complement the complete blockade of 5-HT<sub>2A</sub> serotonin receptors. At a dose of 60 mg, ITI-007 has been shown effective in treating the symptoms associated with schizophrenia, and we believe this higher dose range will be useful for the treatment of bipolar disorder, depressive disorders and other neuropsychiatric diseases.

Given the potential utility for ITI-007 and follow-on compounds to treat these additional indications, we may investigate, either on our own or with a partner, agitation, aggression and sleep disturbances in additional diseases that include autism spectrum disorders; depressive disorder; intermittent explosive disorder; non-motor symptoms and motor complications associated with Parkinson's disease; and post-traumatic stress disorder. We hold exclusive, worldwide commercialization rights to ITI-007 and a family of compounds from Bristol-Myers Squibb Company pursuant to an exclusive license.

*Other Product Candidates*

We have a second major program called ITI-002 that has yielded a portfolio of compounds that selectively inhibits the enzyme phosphodiesterase type 1, or PDE1. We believe PDE1 helps regulate brain activity related to cognition, memory processes and movement/coordination. On February 25, 2011, we (through our wholly owned operating subsidiary, ITI) and Takeda Pharmaceutical Company Limited, or Takeda, entered into a license and collaboration agreement, or the Takeda License Agreement, under which we agreed to collaborate to research, develop and commercialize our proprietary compound ITI-214 and other selected compounds that selectively inhibit PDE1 for use in the prevention and treatment of human diseases. On October 31, 2014, we entered into an agreement with Takeda

terminating the Takeda License Agreement, or the Termination Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to us. On September 15, 2015, Takeda completed the transfer of the Investigational New Drug application, or IND, for ITI-214 to us. ITI-214 is

## **Table of Contents**

the first compound in its class to successfully advance into Phase 1 clinical trials. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's disease, cognition in Alzheimer's disease, cognition in schizophrenia and in other non-CNS indications. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

Our pipeline also includes pre-clinical programs that are focused on advancing drugs for the treatment of schizophrenia, Parkinson's disease, Alzheimer's disease and other neuropsychiatric and neurodegenerative disorders. We are also investigating the development of treatments for disease modification of neurodegenerative disorders and non-CNS diseases.

We have assembled a management team with significant industry experience to lead the discovery and development of our product candidates. We complement our management team with a group of scientific and clinical advisors that includes recognized experts in the fields of schizophrenia and other CNS disorders, including Nobel laureate, Dr. Paul Greengard, one of our co-founders.

Since inception, we have devoted substantially all of our efforts and resources to our research and development activities. We have incurred significant net losses since inception. As of December 31, 2015, our accumulated deficit was \$193.0 million. We expect to continue incurring substantial losses for the next several years as we continue to develop our clinical and pre-clinical drug candidates and programs. Our operating expenses are comprised of research and development expenses and general and administrative expenses.

Our corporate headquarters and laboratory are located in New York, New York.

## **Public Offerings in March 2015 and September 2015**

On March 11, 2015, we completed a public offering of 5,411,481 shares of our common stock at a price of \$24.00 per share for aggregate gross proceeds of approximately \$129.9 million, and net proceeds of approximately \$121.8 million. On September 28, 2015, we completed a public offering of 7,935,000 shares of our common stock at a price of \$43.50 per share for aggregate gross proceeds of approximately \$345.2 million and net proceeds of approximately \$327.4 million.

## **Results of Operations**

### ***Revenues***

The following discussion summarizes the key factors our management believes are necessary for an understanding of our financial statements.

We have not generated any revenue from product sales to date and we do not expect to generate revenues from product sales for at least the next several years. Our revenues for the year ended December 31, 2015 have been from a government grant and the residual reimbursement of expenses from the terminated Takeda License Agreement. Our revenues for the year ended December 31, 2014 have been from the terminated Takeda License Agreement and to a much lesser extent from a government grant. We will not receive any further revenue under the Takeda License Agreement, which was terminated on October 31, 2014. We have received and may continue to receive grants from U.S. government agencies and foundations.

We do not expect any revenues that we may generate in the next several years to be significant enough to fund our operations.



---

**Table of Contents**

***Expenses***

The process of researching and developing drugs for human use is lengthy, unpredictable and subject to many risks. We are unable with any certainty to estimate either the costs or the timelines in which those costs will be incurred. The clinical development of ITI-007 for the treatment of schizophrenia and for the treatment of bipolar depression consumes and will continue to consume a large portion of our current, as well as projected, resources. We intend to pursue other disease indications that ITI-007 may address, but there are significant costs associated with pursuing FDA approval for those indications, which would include the cost of additional clinical trials.

Our ITI-002 program has a compound, ITI-214, in Phase 1 development. We intend to pursue the development of our PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's disease, cognition in Alzheimer's disease, cognition in schizophrenia and in other non-CNS indications. Our other projects are still in the pre-clinical stages, and will require extensive funding not only to complete pre-clinical testing, but to enter into and complete clinical trials. Expenditures that we incur on these projects will be subject to availability of funding in addition to the funding required for the advancement of ITI-007. Any failure or delay in the advancement of ITI-007 could require us to re-allocate resources from our other projects to the advancement of ITI-007, which could have a significant material adverse impact on the advancement of these other projects and on our results of operations. Our operating expenses are comprised of (i) research and development expenses and (ii) general and administrative expenses. Our research and development costs are comprised of:

internal recurring costs, such as labor and fringe benefits, materials and supplies, facilities and maintenance costs; and

fees paid to external parties who provide us with contract services, such as pre-clinical testing, manufacturing and related testing, clinical trial activities and license milestone payments.

General and administrative expenses are incurred in three major categories:

salaries and related benefit costs;

patent, legal and professional costs; and

office and facilities overhead.

We expect that research and development expenses will increase substantially as we proceed with our Phase 3 clinical trials for ITI-007 in patients with exacerbated schizophrenia and our Phase 3 clinical trials for ITI-007 in patients with bipolar disorder. We also expect that our general and administrative costs will increase substantially from prior periods primarily due to costs to perform pre-product commercialization activities and the increased costs associated with being a public reporting entity, which could include adding additional personnel. We granted options to purchase 884,703 shares of our common stock in 2015 and have granted options to purchase an additional 347,137 shares of our common stock in January 2016. We also granted restricted stock units for 5,272 and 78,806 shares of our common stock in December 2015 and January 2016, respectively. We will recognize expense associated with these restricted stock units and options over the next three years in both research and development expenses and general and

administrative expenses. We expect this non-cash expense to be material and affect quarter to quarter and year to date comparisons in the upcoming year. We expect to continue to grant stock options and other stock-based awards in the future, which will increase our stock-based compensation expense in future periods.

**Table of Contents**

The following table sets forth our revenues, operating expenses, interest income (expense) and income taxes expenses for the years ended December 31, 2015, 2014 and 2013 (in thousands):

	<b>For the Year Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
<b>Revenues</b>	<b>\$ 91</b>	<b>\$ 577</b>	<b>\$ 2,737</b>
<b>Expenses</b>			
Research and Development	<b>87,718</b>	21,226	23,028
General and Administrative	<b>18,187</b>	10,338	5,976
	<b>105,905</b>	31,564	29,004
Interest Income (Expense)	<b>1,022</b>	298	(583)
Income Taxes	<b>(1)</b>	(2)	(18)
<b>Net Loss</b>	<b>\$ (104,793)</b>	<b>\$ (30,691)</b>	<b>\$ (26,868)</b>

**Comparison of Years Ended December 31, 2015 and December 31, 2014***Revenues*

Revenues decreased for the year ended December 31, 2015 as compared to the year ended December 31, 2014 by approximately \$485.9 thousand, or 84%, primarily due to reimbursable costs paid to us by Takeda in 2014 under the Takeda License Agreement which terminated on October 31, 2014 with limited reimbursements in 2015, offset by slightly higher revenue in 2015 from a government grant.

*Research and Development Expenses*

Research and development expenses increased for the year ended December 31, 2015 as compared to the year ended December 31, 2014 by approximately \$66.5 million, or 313%. This change is due primarily to an increase of approximately \$47.1 million of costs associated with outside clinical testing and an increase of approximately \$14.9 million from nonclinical testing in the year ended December 31, 2015 over the year ended December 31, 2014. The vast majority of the increase is due to costs associated with conducting our ITI-007 Phase 3 clinical program in schizophrenia. In late 2014, we began a clinical trial of ITI-007 in patients with schizophrenia and incurred the majority of the costs for this trial in 2015. In addition, we started our second Phase 3 clinical trial of ITI-007 in patients with schizophrenia in June 2015 and incurred significant costs for this trial in the second half of 2015. In December 2015, we commenced our Phase 3 clinical trials in bipolar disorder and have incurred approximately \$3.6 million in costs through December 31, 2015. In 2014, we did not incur significant costs related to clinical trials. Amounts paid to external parties comprise a large portion of our research and development costs. In the year ended December 31, 2015, we incurred approximately \$76.8 million of costs to external parties who manufactured, tested and performed clinical trial related activities as compared to \$16.3 million in the year ended December 31, 2014. Of these external costs, approximately \$76.1 million in the year ended December 30, 2015 and \$16.0 million in the year ended December 31, 2014 were for ITI-007 related projects. The remaining amounts for each of these periods were spent on other projects. Internal costs are comprised primarily of labor, fringe benefits, materials, supplies and facilities and maintenance costs and were approximately \$10.9 million and \$5.0 million for the years ended December 31, 2015 and 2014, respectively. The increase in these internal costs is due primarily to hiring additional research and development employees in 2015 in addition to increased stock based compensation expense.

As development of ITI-007 for the treatment of schizophrenia progresses, we anticipate costs for that program to increase considerably in the next several years as we continue to conduct Phase 3 and other clinical trials. We are also required to complete non-clinical testing to obtain FDA approval and manufacture material needed for clinical trial use, which includes non-clinical testing of the drug product and the creation of an inventory of drug product in anticipation of possible FDA approval. In addition we plan to spend increasing amounts to further our development of ITI-007 for other indications, including but not limited to, the treatment of

**Table of Contents**

depressive episodes associated with bipolar disorder (bipolar depression), for treatment of behavioral disturbances associated with dementia and related disorders, and for treating agitation, aggression and sleep disturbances in diseases that include dementia, Alzheimer's disease, Huntington's disease and autism spectrum disorders, among other indications.

As of December 31, 2015, we employed 24 full time personnel in our research and development group as compared to 16 full time personnel at December 31, 2014. We expect to hire additional staff as we increase our development efforts and grow our business in the upcoming years.

We currently have several projects, in addition to ITI-007, that are in the research and development stages, including in the areas of cognitive dysfunction and the treatment of neurodegenerative diseases, including Alzheimer's disease, among others. We have used internal resources and incurred expenses not only in relation to the development of ITI-007, but also in connection with these additional projects as well. We have not, however, reported these costs on a project by project basis, as these costs are broadly spread among these projects. The external costs for these projects have been minimal and are reflected in the amounts discussed in this section – Research and Development Expenses.

During previous years, we also incurred costs that were both reimbursable and non-reimbursable under the Takeda License Agreement. For the years ended December 31, 2015 and 2014, we incurred \$30,700 and \$14,000, respectively, of costs that were billable to Takeda pursuant to ongoing obligations under the termination agreement. We do not expect to incur material costs going forward under this agreement.

The research and development process necessary to develop a pharmaceutical product for commercialization is subject to extensive regulation by numerous governmental authorities in the United States and other countries. This process typically takes years to complete and requires the expenditure of substantial resources. The steps required before a drug may be marketed in the United States generally include the following:

completion of extensive pre-clinical laboratory tests, animal studies, and formulation studies in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;

submission to the FDA of an Investigational New Drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin;

performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each proposed indication;

submission to the FDA of a New Drug Application, or NDA, after completion of all clinical trials;

satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient, or API, and finished drug product are produced and tested to assess compliance with current Good Manufacturing Practices, or cGMPs;

satisfactory completion of FDA inspections of clinical trial sites to assure that data supporting the safety and effectiveness of product candidates has been generated in compliance with Good Clinical Practices; and

FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

The successful development of our product candidates and the approval process requires substantial time, effort and financial resources, and is uncertain and subject to a number of risks. We cannot be certain that any of our product candidates will prove to be safe and effective, will meet all of the applicable regulatory requirements needed to receive and maintain marketing approval, or will be granted marketing approval on a timely basis, if at all. Data from pre-clinical studies and clinical trials are susceptible to varying interpretations that could delay, limit or prevent regulatory approval or could result in label warnings related to or recalls of approved products.

---

**Table of Contents**

We, the FDA, or other regulatory authorities may suspend clinical trials at any time if we or they believe that the subjects participating in such trials are being exposed to unacceptable risks or if such regulatory agencies find deficiencies in the conduct of the trials or other problems with our product candidates. Other risks associated with our product candidates are described in the section entitled *Risk Factors* in this Annual Report on Form 10-K.

*General and Administrative Expenses*

General and administrative expenses increased for the year ended December 31, 2015 as compared to the year ended December 31, 2014 by approximately \$7.8 million, or 76%, primarily due to approximately \$4.1 million of higher stock option expense and to a much lesser extent to increased bonus and labor costs and state and local franchise and capital taxes. Salaries, bonuses and related benefit costs for our executive, finance and administrative functions for the years ended December 31, 2015 and 2014 were approximately 59% and 49%, respectively, of our total general and administrative costs. Our other general and administrative expenses include patent costs, legal, accounting and other professional fees and, to a lesser extent, facilities and general office-related overhead.

We expect general and administrative costs to increase significantly as we hire additional staff, expand our operations, including initial preparation for potential commercial activities, and incur additional costs associated with the requirements of Section 404 of the Sarbanes-Oxley Act of 2002 in addition to being a public company and complying with exchange listing and SEC requirements, including the additional complexities and related costs of our transition at the end of 2015 from an emerging growth company to a large accelerated filer under the rules of the SEC. These increases could include higher legal fees, accounting fees and fees associated with investor relations activities, among others.

*Interest Income*

Interest income has increased to approximately \$1.0 million from \$304,000 for the year ended December 31, 2015 as compared to the year ended December 31, 2014. This increase is primarily a result of higher than average cash balances in 2015 as compared to 2014 which is due to the net offering proceeds of \$121.8 million that we received in March 2015 and \$327.4 million that we received in September 2015.

*Comparison of Years Ended December 31, 2014 and December 31, 2013**Revenues*

Revenue decreased for the year ended December 31, 2014 as compared to the year ended December 31, 2013 by approximately \$2.2 million, or 79%, due primarily to the recognition in 2013 of previously deferred revenue relating to the Takeda License Agreement and lower reimbursable costs payable to us by Takeda in 2014 under the Takeda License Agreement, offset to a much lesser extent by revenue from a government grant in 2014.

*Research and Development Expenses*

Research and development expenses decreased for the year ended December 31, 2014 as compared to the year ended December 31, 2013 by approximately \$1.8 million, or 8%. This decrease is due primarily to costs associated with outside clinical testing for our ITI-007 Phase 2 clinical trial that was completed in late 2013 as compared to costs incurred in conducting our ITI-007 Phase 3 clinical trial, which began in the fourth quarter of 2014. Partially offsetting this decrease were expenses of approximately \$6.6 million incurred in 2014 as compared to \$1.9 million in 2013 related to the manufacturing and other clinical and non-clinical testing of our ITI-007 product candidate and expenses of approximately \$1.9 million related to our ITI-007-200 Phase 1/2 clinical trial in healthy geriatric and

dementia patients incurred only in 2014. In addition, stock option expense increased by \$1.7 million for the year ended December 31, 2014 due primarily to stock options granted in 2014.



---

**Table of Contents**

The research and development expenses incurred for amounts payable to external parties comprised a significant portion of our research and development expenses during the years ended December 31, 2014 and 2013. We incurred expenses of approximately \$14.8 million and \$18.8 million for the years ended December 31, 2014 and 2013, respectively, for amounts payable to external parties who manufactured, tested and performed clinical trial activities for all of our projects. We spent approximately \$14.4 million and \$18.3 million on external costs for the development of ITI-007 for the years ended December 31, 2014 and 2013, respectively. During the same periods, our internal research and development expenses for all projects were approximately \$5.0 million and \$3.0 million, respectively. The clinical development work related to ITI-007 requires the largest portion of our resources and, consequently, comprises the majority of our spending. For the years ended December 31, 2014 and 2013, we incurred total expenses of \$18.8 million and \$20.8 million, respectively, for all ITI-007 related projects and \$2.4 million and \$2.2 million, respectively, for all of our other projects. Total research and development expenses were approximately \$21.2 million for the year ended December 31, 2014 as compared to \$23.0 million for 2013.

During 2014 and in previous years, we also incurred costs that were both reimbursable and non-reimbursable under the Takeda License Agreement. For the year ended December 31, 2014, we incurred approximately \$14,000 on direct costs that were billable to Takeda as compared to \$97,000 for the year ended December 31, 2013.

*General and Administrative Expenses*

General and administrative expenses increased for the year ended December 31, 2014 as compared to the year ended December 31, 2013 by approximately \$4.4 million, or 73%. This increase was primarily due to increased stock option expense of \$1.7 million in 2014 related to options granted in 2014, and increased labor and related benefit costs of approximately \$0.6 million, with the remainder comprised of higher professional fees, directors and officers insurance costs, and board of directors compensation fees, which are due to the activities associated with being a public company. We expect these costs to increase significantly as we expand our operations, including hiring of additional personnel, continue to be subject to the reporting requirements of being a public company and issue additional equity incentive awards.

**Liquidity and Capital Resources**

Through December 31, 2015, we provided funds for our operations by obtaining approximately \$716.3 million of cash primarily through public and private offerings of our common stock and other securities, grants from government agencies and foundations and payments received under the terminated Takeda License Agreement. We do not believe that grant revenue will be a significant source of funding in the near future, and Takeda has limited ongoing funding obligations following the termination of the Takeda License Agreement on October 31, 2014. On March 11, 2015, we completed a public offering of 5,411,481 shares of our common stock for aggregate gross proceeds of approximately \$129.9 million and net proceeds of approximately \$121.8 million. On September 28, 2015, we completed an additional public offering of 7,935,000 shares of our common stock for aggregate gross proceeds of approximately \$345.2 million and net proceeds of approximately \$327.4 million.

As of December 31, 2015, we had a total of approximately \$475.2 million in cash and cash equivalents and available-for-sale investment securities, and approximately \$6.3 million of short-term liabilities consisting entirely of liabilities from operations. Excluding the increase in net cash of approximately \$121.8 million and \$327.4 million from the public offerings in March 2015 and September 2015, respectively, we spent approximately \$103.1 million in cash for operations and equipment and we reduced working capital by approximately \$92.7 million for the year ended December 31, 2015. This use of cash was primarily for conducting clinical trials and non-clinical testing, including manufacturing related activities and funding recurring operating expenses.



---

**Table of Contents**

For the year 2016, we expect to spend between approximately \$130 million and \$160 million. We expect these expenditures to be due primarily to the development of ITI-007 in patients with schizophrenia, behavioral disturbances in dementia, bipolar disorder and depressive disorders, our ITI-007 long acting injectable development program through pre-clinical and early clinical development, research and preclinical development of our other product candidates, the continuation of manufacturing activities in connection with the development of ITI-007, recurring expenses and costs to produce, develop and validate materials to be used in clinical and non-clinical studies related to ITI-007, and expenses associated with our other development programs and general operations. We expect that cash expenditures will continue to increase after 2016 as we further expand the ITI-007 clinical stage programs, the ITI-007 long acting injectable development program through pre-clinical and early clinical development; research and preclinical development of our other product candidates; the continuation of manufacturing, pre-commercial activities in connection with the development of ITI-007 and the early stage pre-commercial launch activities for ITI-007. We believe that our existing cash and cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements through the end of 2018.

We will require significant additional financing in the future to continue to fund our operations. We believe that we have the funding in place to complete the additional clinical and non-clinical trials, manufacturing and pre-commercialization activities needed for potential regulatory approval and commercialization of ITI-007 in patients with schizophrenia. With the remaining proceeds from our public offerings in March 2015 and September 2015, we believe that we have the funds to complete our proposed clinical trials of ITI-007 in bipolar disorder as a monotherapy and as an adjunctive therapy with lithium or valproate. We will also be funding clinical trials of ITI-007 for the treatment of behavioral disturbances in dementia; preclinical and clinical development of ITI-007 long acting injectable development program; additional clinical trials of ITI-007; continued clinical development of our PDE program, including ITI-214; research and preclinical development of our other product candidates; and the continuation of manufacturing activities in connection with the development of ITI-007. We anticipate requiring additional funds to obtain regulatory approval for ITI-007 in patients with dementia, including Alzheimer's disease, for further development of ITI-007 in patients with bipolar disorder, depressive disorders and other indications, and for development of our other product candidates. We have incurred losses in every year since inception with the exception of 2011, when we received an up-front fee and a milestone payment related to the Takeda License Agreement. These losses have resulted in significant cash used in operations. For the year ended December 31, 2015, we used net cash in operating activities and purchases of equipment of approximately \$103.1 million and expect to use additional cash of between approximately \$130 and \$160 million through the end of 2016. While we have several research and development programs underway, the ITI-007 program has advanced the furthest and will continue to consume increasing amounts of cash for conducting clinical trials and the testing and manufacturing of product material. As we continue to conduct the activities necessary to pursue FDA approval of ITI-007 and our other product candidates, we expect the amount of cash needed to fund operations to increase significantly over the next several years.

With the termination of the Takeda License Agreement in October 2014, we will not receive milestone payments and only limited expense reimbursements, including patent filing costs, from Takeda and will be responsible for the costs of developing ITI-214. On September 15, 2015, Takeda completed the transfer of the IND for ITI-214 to us. We intend to pursue the development of our PDE1 program, including ITI-214 for the treatment of several CNS and non-CNS conditions, but we do not anticipate a significant increase in our operating expenses related to our PDE development programs through at least the first half of 2016.

We seek to balance the level of cash, cash equivalents and investments on hand with our projected needs and to allow us to withstand periods of uncertainty relative to the availability of funding on favorable terms. Until we can generate significant revenues from operations, we will need to satisfy our future cash needs through public or private sales of our equity securities, sales of debt securities, the incurrence of debt from commercial lenders, strategic collaborations, licensing a portion or all of our product candidates and technology and, to a lesser extent, grant funding.



## **Table of Contents**

We cannot be sure that future funding will be available to us when we need it on terms that are acceptable to us, or at all. We sell securities and incur debt when the terms of such transactions are deemed favorable to us and as necessary to fund our current and projected cash needs. The amount of funding we raise through sales of our common stock or other securities depends on many factors, including, but not limited to, the status and progress of our product development programs, projected cash needs, availability of funding from other sources, our stock price and the status of the capital markets. Due to the volatile nature of the financial markets, equity and debt financing may be difficult to obtain. In addition, any unfavorable development or delay in the progress of our ITI-007 program could have a material adverse impact on our ability to raise additional capital.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

If adequate funds are not available to us on a timely basis, we may be required to: (1) delay, limit, reduce or terminate pre-clinical studies, clinical trials or other clinical development activities for one or more of our product candidates, including our lead product candidate ITI-007, ITI-214, and our other pre-clinical stage product candidates; (2) delay, limit, reduce or terminate our discovery research or pre-clinical development activities; or (3) enter into licenses or other arrangements with third parties on terms that may be unfavorable to us or sell, license or relinquish rights to develop or commercialize our product candidates, technologies or intellectual property at an earlier stage of development and on less favorable terms than we would otherwise agree.

Our cash is maintained in checking accounts, money market accounts, money market mutual funds, U.S. government agency securities, certificates of deposit, commercial paper, corporate notes and corporate bonds at major financial institutions. Due to the current low interest rates available for these instruments, we are earning limited interest income. We do not expect interest income to be a significant source of funding over the next several quarters. Our investment portfolio has not been adversely impacted by the problems in the credit markets that have existed over the last several years, but there can be no assurance that our investment portfolio will not be adversely affected in the future.

In 2014, we entered into a long-term lease, which was amended in December 2015, for 16,753 square feet of useable laboratory and office space located at 430 East 29th Street, New York, New York 10016. Due to the amortization of total lease payments, we have recognized \$1.6 million of deferred rent in the year ended December 31, 2015. The deferred rent balance will incrementally increase over approximately the next year. We occupied these facilities as our headquarters in March 2015, replacing our previous laboratories and offices. The lease, as amended, has a term of 12 years. We expect that our facility related costs will increase moderately as a result of leasing this facility.

## **Off-Balance Sheet Arrangements**

We do not have any off-balance sheet arrangements.

**Table of Contents****Contractual Obligations and Commitments**

Total contractual obligations as of December 31, 2015 are summarized in the following table (in thousands):

	<b>Total</b>	<b>Payments Due By Period</b>			
		<b>Less than 1 Year</b>	<b>1-3 Years</b>	<b>4-5 Years</b>	<b>More than 5 Years</b>
Operating Lease Obligations	\$ 16,256	\$ 0	\$ 4,257	\$ 3,138	\$ 8,861

The table of Contractual Obligations and Commitments does not reflect that, under the License Agreement with BMS, we may be obligated to make future milestone payments to BMS totaling \$12 million; to make other future milestone payments to BMS for each licensed product of up to an aggregate of approximately \$14.75 million; to make tiered single digit percentage royalty payments on sales of licensed products; and to pay BMS a percentage of non-royalty payments made in consideration of any sublicense.

**Critical Accounting Policies and Estimates**

The discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires management to make estimates and assumptions that affect reported amounts of assets and liabilities as of the date of the balance sheet and reported amounts of revenues and expenses for the periods presented. Judgments must also be made about the disclosure of contingent liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management makes estimates and exercises judgment in revenue recognition and stock-based compensation. Actual results may differ from those estimates and under different assumptions or conditions.

We believe that the following critical accounting policies affect management's more significant judgments and estimates used in the preparation of our financial statements:

***Revenue Recognition***

Revenue is recognized when all terms and conditions of the agreements have been met, including that persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable and collectability is reasonably assured. We are reimbursed for certain costs incurred on specified research projects under the terms and conditions of grants, collaboration agreements, and awards. We record the amount of reimbursement as revenues on a gross basis in accordance with ASC Topic 605-45, *Revenue Recognition/Principal Agent Considerations*. We are the primary obligor with respect to purchasing goods and services from third-party suppliers, are obligated to compensate the service provider for the work performed, and have discretion in selecting the supplier. Provisions for estimated losses on research grant projects and any other contracts are made in the period such losses are determined.

We have entered into arrangements involving the delivery of more than one element. Each required deliverable is evaluated to determine whether it qualifies as a separate unit of accounting. For us, this determination is generally based on whether the deliverable has stand-alone value to the customer. We adopted this accounting standard on a prospective basis for all Multiple-Deliverable Revenue Arrangements, or MDRAs, entered into on or after January 1,

2011, and for any MDRAs that were entered into prior to January 1, 2011, but materially modified on or after that date.

## **Table of Contents**

The adoption of this accounting standard did not have a material impact on our results of operations for the years ended December 31, 2015, 2014 and 2013, or on our financial positions as of those dates.

We have adopted ASC Topic 605-28, *Milestone Method*. Under this guidance, we recognize revenue contingent upon the achievement of a substantive milestone in its entirety in the period the milestone is achieved. Substantive milestone payments are recognized upon achievement of the milestone only if all of the following conditions are met:

the milestone payments are non-refundable;

achievement of the milestone involves a degree of risk and was not reasonably assured at the inception of the arrangement;

substantive effort on our part is involved in achieving the milestone;

the amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and

a reasonable amount of time passes between the up-front license payment and the first milestone payment, as well as between each subsequent milestone payment.

Determination as to whether a payment meets the aforementioned conditions involves management's judgment. If any of these conditions are not met, the resulting payment would not be considered a substantive milestone, and therefore, the resulting payment would be considered part of the consideration for the single unit of accounting and be recognized as revenue as such performance obligations are performed under either the proportional performance or straight-line methods, as applicable. In addition, the determination that one such payment was not a substantive milestone could prevent us from concluding that subsequent milestone payments were substantive milestones and, as a result, any additional milestone payments could also be considered part of the consideration for the single unit of accounting and would be recognized as revenue as such performance obligations are performed under either the proportional performance or straight-line methods, as applicable.

## ***Research and Development***

Except for payments made in advance of services, the Company expenses its research and development costs as incurred. For payments made in advance, the Company recognizes research and development expense as the services are rendered. Research and development costs primarily consist of salaries and related expenses for personnel and resources and the costs of clinical trials. Other research and development expenses include preclinical analytical testing, outside services, providers, materials and consulting fees.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to the Company by its vendors with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.



As part of the process of preparing its financial statements, the Company is required to estimate its expenses resulting from its obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company's objective is to reflect the appropriate trial expenses in its financial statements by matching those expenses with the period in which services are performed and efforts are expended. The Company accounts for these expenses according to the progress of the trial as measured by subject progression and the timing of various aspects of the trial. The

---

**Table of Contents**

Company determines accrual estimates through financial models taking into account discussion with applicable personnel and outside service providers as to the progress or state of consummation of trials, or the services completed. During the course of a clinical trial, the Company adjusts its clinical expense recognition if actual results differ from its estimates. The Company makes estimates of its accrued expenses as of each balance sheet date based on the facts and circumstances known to it at that time. The Company's clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in it reporting amounts that are too high or too low for any particular period.

***Stock-Based Compensation***

Stock-based payments in the form of options are accounted for in accordance with the provisions of ASC Topic 718, *Compensation - Stock Compensation*. The fair value of share-based payments is estimated, on the date of grant, using the Black-Scholes-Merton option-pricing model, or the Black-Scholes model. The resulting fair value is recognized ratably over the requisite service period, which is generally the vesting period of the option. Restricted stock units are valued at the fair market value on the date of grant as determined by the closing stock price.

For all awards granted with time-based vesting conditions, expense is amortized using the straight-line attribution method. For awards that contain a performance-based vesting condition, expense is amortized using the accelerated attribution method. Share-based compensation expense recognized in the statements of operations for the years ended December 31, 2015, 2014 and 2013 is based on share-based awards ultimately expected to vest, and this amount has therefore been reduced for estimated forfeitures. ASC Topic 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Pre-vesting forfeitures for the fiscal years ended December 31, 2015, 2014 and 2013 were estimated based on our historical experience and have not been material.

We utilize the Black-Scholes model for estimating fair value of our stock options granted. Option valuation models, including the Black-Scholes model, require the input of subjective assumptions, and changes in the assumptions used can materially affect the grant date fair value of an award. These assumptions include the risk-free rate of interest, expected dividend yield, expected volatility and the expected life of the award. Restricted stock units are valued at the fair market value on the date of grant as determined by the closing stock price.

Expected volatility rates are based on historical volatility of the common stock of comparable publicly traded entities and other factors due to the limited historical information about our common stock. The expected life of stock options is the period of time for which the stock options are expected to be outstanding. Given the limited historical exercise data, the expected life is determined using the simplified method, which is defined as the midpoint between the vesting date and the end of the contractual term.

The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. We have not paid dividends to our stockholders since our inception and do not plan to pay cash dividends in the foreseeable future. Therefore, we have assumed an expected dividend rate of zero.

Prior to January 1, 2014, given that there was no active market for our common stock, the exercise price of the stock options on the date of grant was determined and approved by the board of directors using several factors, including progress and milestones achieved in our business development and performance, the price per share of our convertible preferred stock offerings and general industry and economic trends. In establishing the estimated fair value of our common stock, we considered the guidance set forth in American Institute of Certified



## **Table of Contents**

Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. For stock options granted in 2014 and 2015, the exercise price was determined by using the closing market price of our common stock on the date of grant.

Under ASC Topic 718, the cumulative amount of compensation cost recognized for instruments classified as equity that ordinarily would result in a future tax deduction under existing tax law shall be considered to be a deductible difference in applying ASC Topic 740, *Income Taxes*. The deductible temporary difference is based on the compensation cost recognized for financial reporting purposes. However, these provisions currently do not impact us, as all the deferred tax assets have a full valuation allowance.

Since we had net operating loss carryforwards as of December 31, 2015, 2014 and 2013, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations.

Equity instruments issued to non-employees are accounted for under the provisions of ASC Topic 718 and ASC Topic 505-50, *Equity/Equity-Based Payments to Non-Employees*. Accordingly, the estimated fair value of the equity instrument is recorded on the earlier of the performance commitment date or the date the services required are completed and are marked to market during the service period.

## **Recently Issued Accounting Pronouncements**

We review new accounting standards to determine the expected financial impact, if any, that the adoption of each such standard will have.

In November 2015, the FASB issued Accounting Standards Update No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes*. Current GAAP requires an entity to separate deferred income tax liabilities and assets into current and noncurrent amounts in a classified statement of financial position. To simplify the presentation of deferred income taxes, ASU 2015-17 requires that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. The current requirement that deferred tax liabilities and assets of a tax-paying component of an entity be offset and presented as a single amount is not affected by the amendments in this Update. The amendments in this Update are effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Earlier application is permitted for all entities as of the beginning of an interim or annual reporting period. We have elected to adopt this update as of the fourth quarter of 2015, retrospectively. The adoption of this standard did not have a material impact on our consolidated financial statements and accompanying notes.

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update No. 2014-09 (ASU 2014-09), *Revenue from Contracts with Customers*. ASU 2014-09 will eliminate transaction-specific and industry-specific revenue recognition guidance under current GAAP and replace it with a principle-based approach for determining revenue recognition. ASU 2014-09 will require that companies recognize revenue based on the value of transferred goods or services as they occur in the contract. ASU 2014-09 also will require additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. In July 2015, the FASB decided to defer the effective date of the standard from January 1, 2017, to January 1, 2018, with an option that permits companies to adopt the standard as early as the original effective date. Early application prior to the original effective date is not permitted. The standard permits the use of either the retrospective or cumulative effect transition method. Presently, we are assessing what effect the adoption of this standard will have on our consolidated financial statements and accompanying notes.



**Table of Contents****Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

*Interest Rate Sensitivity.* As of December 31, 2015, we had cash, cash equivalents and marketable securities of \$475.2 million consisting of cash deposited in a highly rated financial institution in the United States and in a short-term U.S. Treasury money market fund, as well as high-grade corporate bonds and commercial paper. The primary objective of our investment activities is to preserve our capital for the purpose of funding operations and we do not enter into investments for trading or speculative purposes. We believe that we do not have material exposure to high-risk investments such as mortgage-backed securities, auction rate securities or other special investment vehicles within our money-market fund investments. We believe that we do not have any material exposure to changes in fair value as a result of changes in interest rates, although the recent rise in interest rates has resulted in our unrealized loss on investments for the year ended December 31, 2015 and 2014 totaling approximately \$0.5 million and \$0.1 million, respectively. Since we plan on holding those investments to maturity, no recognition of impairment is required. Declines in interest rates, however, would reduce future investment income.

*Capital Market Risk.* We currently have no product revenues and depend on funds raised through other sources. One possible source of funding is through further equity offerings. Our ability to raise funds in this manner depends upon capital market forces affecting our stock price.

**Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA  
INTRA-CELLULAR THERAPIES, INC.**

	Number
<u>Index to Financial Statements and Financial Statement Schedules</u>	
<u>Independent Auditors Report</u>	F-1
<u>Consolidated Balance Sheets as of December 31, 2015 and 2014</u>	F-2
<u>Consolidated Statements of Operations for the Years Ended December 31, 2015, 2014 and 2013</u>	F-3
<u>Consolidated Statements of Comprehensive Loss for the Years Ended December 31, 2015, 2014 and 2013</u>	F-4
<u>Consolidated Statements of Stockholders Equity for the Years Ended December 31, 2015, 2014 and 2013</u>	F-5
<u>Consolidated Statements of Cash Flows for the Years Ended December 31, 2015, 2014 and 2013</u>	F-6
<u>Notes to Consolidated Financial Statements</u>	F-7

**Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

Not applicable.

**Item 9A. CONTROLS AND PROCEDURES****Evaluation of Disclosure Controls and Procedures**

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

## **Table of Contents**

### **Management's Report on Internal Control over Financial Reporting**

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, as a process designed by, or under the supervision of, the Company's principal executive and principal financial officers and effected by the Company's board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. The Company's internal control over financial reporting includes those policies and procedures that:

pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company;

provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and

provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

The Company's management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2015. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013).

Based on our assessment, management believes that, as of December 31, 2015, the company's internal control over financial reporting is effective based on those criteria.

Our independent registered public accounting firm has issued an audit report on our assessment of our internal control over financial reporting. This report appears further below in this Item 9A.

### **Changes in Internal Controls**

There were no changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control that occurred during the fourth quarter of our last fiscal year that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting other than our continued improvement of documentation and other existing internal controls. This improvement included but was not limited to hiring additional personnel, hiring an independent outside firm to aid in the controls testing and reassigning tasks to allow for greater segregation of duties.



**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders of Intra-Cellular Therapies, Inc.

We have audited Intra-Cellular Therapies, Inc. and subsidiaries' internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Intra-Cellular Therapies, Inc. and subsidiaries' management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial

**Table of Contents**

reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Intra-Cellular Therapies, Inc. and subsidiaries maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Intra-Cellular Therapies, Inc. and subsidiaries as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2015 and our report dated February 25, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Baltimore, MD

February 25, 2016

**Item 9B. OTHER INFORMATION**

Not applicable.



**Table of Contents**

**PART III**

**Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The response to this item is incorporated by reference from the discussion responsive thereto under the captions Management and Corporate Governance, Section 16(a) Beneficial Ownership Reporting Compliance, and Code of Conduct and Ethics in the Company's Proxy Statement for the 2016 Annual Meeting of Stockholders.

**Item 11. EXECUTIVE COMPENSATION**

The response to this item is incorporated by reference from the discussion responsive thereto under the captions Executive Officer and Director Compensation, Compensation Discussion and Analysis, Management and Corporate Governance Compensation Committee Interlocks and Insider Participation, Compensation Committee Report and Compensation Practices and Policies Relating to Risk Management in the Company's Proxy Statement for the 2016 Annual Meeting of Stockholders.

**Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The response to this item is incorporated by reference from the discussion responsive thereto under the captions Security Ownership of Certain Beneficial Owners and Management and Equity Compensation Plan Information in the Company's Proxy Statement for the 2016 Annual Meeting of Stockholders.

**Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

The response to this item is incorporated by reference from the discussion responsive thereto under the captions Certain Relationships and Related Person Transactions and Management and Corporate Governance in the Company's Proxy Statement for the 2016 Annual Meeting of Stockholders.

**Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

The response to this item is incorporated by reference from the discussion responsive thereto under the caption Proposal 2: Ratification of Selection of Independent Registered Public Accounting Firm in the Company's Proxy Statement for the 2016 Annual Meeting of Stockholders.

**Table of Contents****PART IV****Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES**

**Item 15(a).** The following documents are filed as part of this annual report on Form 10-K:

**Item 15(a)(1) and (2)** See Index to Consolidated Financial Statements and Financial Statement Schedules at Item 8 to this Annual Report on Form 10-K. Other financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.

**Item 15(a)(3)** Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

<b>Exhibit Number</b>	<b>Exhibit Description</b>	<b>Filed Herewith</b>	<b>Incorporated by Reference herein from Form or Schedule</b>	<b>Filing Date</b>	<b>SEC File/Reg. Number</b>
2.1	Agreement and Plan of Merger, dated as of August 23, 2013, by and among the Registrant, ITI, Inc. and Intra-Cellular Therapies, Inc.		8-K (Exhibit 2.1)	8/29/2013	000-54896
2.2	Agreement and Plan of Merger, dated as of August 29, 2013, by and between the Registrant and Intra-Cellular Therapies, Inc., relating to the name change of the Registrant.		8-K (Exhibit 2.2)	9/5/2013	000-54896
3.1	Restated Certificate of Incorporation of the Registrant, filed with the Secretary of State of the State of Delaware on November 7, 2013.		S-1/A (Exhibit 3.1)	11/26/13	333-191238
3.2	Certificate of Merger relating to the Merger of ITI, Inc. with and into Intra-Cellular Therapies, Inc., filed with the Secretary of State of the		8-K (Exhibit 3.3)	9/5/2013	000-54896

Edgar Filing: Intra-Cellular Therapies, Inc. - Form 10-K

State of Delaware on August 29, 2013.

3.3	Certificate of Ownership and Merger relating to the Merger of Intra-Cellular Therapies, Inc. with and into the Registrant, filed with the Secretary of State of the State of Delaware on August 29, 2013, relating to the name change of the Registrant.	8-K  (Exhibit 3.4)	9/5/2013	000-54896
3.4	Restated Bylaws of the Registrant.	8-K  (Exhibit 3.5)	9/5/2013	000-54896
4.1	Form of common stock certificate.	8-K  (Exhibit 4.1)	9/5/2013	000-54896
4.2	.1 Warrant to Purchase Common Stock dated April 19, 2013 issued to Alzheimer Drug Discovery Foundation, Inc.	8-K  (Exhibit 4.2.1)	9/5/2013	000-54896

**Table of Contents**

<b>Exhibit Number</b>	<b>Exhibit Description</b>	<b>Filed Herewith</b>	<b>Incorporated by Reference herein from Form or Schedule</b>	<b>Filing Date</b>	<b>SEC File/Reg. Number</b>
	.2 Amendment dated August 29, 2013 to Warrant to Purchase Common Stock dated April 19, 2013 issued to Alzheimer Drug Discovery Foundation, Inc.		8-K (Exhibit 4.2.2)	9/5/2013	000-54896
10.1	.1 License Agreement dated as of May 31, 2005 by and between Bristol-Meyers Squibb Company and Intra-Cellular Therapies, Inc.**		8-K/A (Exhibit 10.1.1)	10/31/2013	000-54896
	.2 Amendment No. 1 to License Agreement dated as of November 3, 2010 by and between Bristol-Meyers Squibb Company and Intra-Cellular Therapies, Inc.		8-K (Exhibit 10.1.2)	9/5/2013	000-54896
10.2	.1 License and Collaboration Agreement dated as of February 25, 2011 by and between Takeda Pharmaceutical Company Limited and Intra-Cellular Therapies, Inc.**		8-K/A (Exhibit 10.2)	10/31/2013	000-54896
	.2 Termination Agreement dated as of October 31, 2014 by and between Takeda Pharmaceutical Company Limited and Intra-Cellular Therapies, Inc.		10-K (Exhibit 10.2.2)	3/12/2015	001-36274
10.3	Employment Agreement effective as of February 26, 2008 by and between Sharon Mates, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.3)	9/5/2013	000-54896
10.4	Employment Agreement effective as of August 3, 2015 by and between Michael I. Halstead and Intra-Cellular Therapies, Inc..*		10-Q (Exhibit 10.1)	11/5/2015	001-36274
10.5	Employment Agreement effective as of February 26, 2008 by and between Lawrence J. Hinline and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.4)	9/5/2013	000-54896
10.6	Employment Agreement effective as of November 4, 2015 by and between Robert Davis, Ph.D. and Intra-Cellular Therapies, Inc.*	X			

10.7	Employment Agreement effective as of November 5, 2015 by and between Kimberly Vanover, Ph.D. and Intra-Cellular Therapies, Inc.*	X
------	---	---



**Table of Contents**

<b>Exhibit Number</b>	<b>Exhibit Description</b>	<b>Filed Herewith</b>	<b>Incorporated by Reference herein from Form or Schedule</b>	<b>Filing Date</b>	<b>SEC File/Reg. Number</b>
10.8	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of September 1, 2003 by and between Sharon Mates, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.8)	9/5/2013	000-54896
10.9	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of July 29, 2014 by and between Michael Halstead and Intra-Cellular Therapies, Inc.*		10-K (Exhibit 10.11)	3/12/2015	001-36274
10.10	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of December 1, 2003 by and between Lawrence J. Hineline and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.9)	9/5/2013	000-54896
10.11	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of November 4, 2015 by and between Robert Davis, Ph.D. and Intra-Cellular Therapies, Inc.*	X			
10.12	Employee Proprietary Information, Inventions, and Non-Competition Agreement effective as of March 5, 2007 by and between Kimberly E. Vanover, Ph.D. and Intra-Cellular Therapies, Inc.*		8-K (Exhibit 10.12)	9/5/2013	000-54896
10.13	Form of Indemnification Agreement by and between the Company and its directors and executive officers.*		8-K (Exhibit 10.13)	9/5/2013	000-54896
10.14	2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.14)	9/5/2013	000-54896
10.15	Form of Stock Option Agreement under the 2003 Equity Incentive Plan, as amended.*		8-K (Exhibit 10.15)	9/5/2013	000-54896
10.16	Amended and Restated 2013 Equity Incentive Plan.*		8-K (Exhibit 10.1)	6/18/2015	001-36274

Edgar Filing: Intra-Cellular Therapies, Inc. - Form 10-K

10.17	Form of Stock Option Agreement under the 2013 Equity Incentive Plan.*	10-K (Exhibit 10.19)	3/25/2014	001-36274
10.18	Non-Employee Director Compensation Policy.*	10-Q (Exhibit 10.1)	8/12/2014	001-36274

**Table of Contents**

<b>Exhibit Number</b>	<b>Exhibit Description</b>	<b>Filed Herewith</b>	<b>Incorporated by Reference herein from Form or Schedule</b>	<b>Filing Date</b>	<b>SEC File/Reg. Number</b>
10.19	Redemption Agreement dated as of August 29, 2013 by and between the Registrant and NLBDIT 2010 Services, LLC.		8-K (Exhibit 10.17)	9/5/2013	000-54896
10.20	Indemnity Agreement dated as of August 29, 2013 by and among the Registrant, Intra-Cellular Therapies, Inc. and Samir N. Masri.		8-K (Exhibit 10.18)	9/5/2013	000-54896
10.21	Registration Rights Agreement dated as of August 29, 2013 by and among Intra-Cellular Therapies, Inc., the stockholders named therein and the Registrant.		8-K (Exhibit 10.19)	9/5/2013	000-54896
14.1	Corporate Code of Conduct and Ethics and Whistleblower Policy.	X			
21.1	Subsidiaries.		S-1 (Exhibit 21.1)	9/18/13	333-191238
23.1	Consent of Ernst & Young LLP.	X			
31.1	Certification of the Chief Executive Officer.	X			
31.2	Certification of the Chief Financial Officer.	X			
32.1	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101	.INS XBRL Instance Document.	X			
	.SCH XBRL Taxonomy Extension Schema Document.	X			
	.CAL XBRL Taxonomy Extension Calculation Linkbase Document.	X			
	.DEF XBRL Taxonomy Extension Definition.	X			
	.LAB XBRL Taxonomy Extension Label Linkbase Document.	X			
	.PRE XBRL Taxonomy Presentation Linkbase Document.	X			

- \* Management contract or compensatory plan or arrangement.
- \*\* Confidential treatment has been granted for portions of this Exhibit. Redacted portions filed separately with the Securities and Exchange Commission.  
Confidential treatment is being requested for portions of this Exhibit. Redacted portions filed separately with the Securities and Exchange Commission.

Table of Contents**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**INTRA-CELLULAR THERAPIES, INC.**

Date: February 25, 2016

By: /s/ Sharon Mates, Ph.D.

Sharon Mates, Ph.D.

Chairman, President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated below and on the dates indicated.

	Signatures	Title	Date
By:	/s/ Sharon Mates, Ph.D. Sharon Mates, Ph.D.	Chairman, President and Chief Executive Officer (principal executive officer)	February 25, 2016
By:	/s/ Lawrence J. Himeline Lawrence J. Himeline	Vice President of Finance and Chief Financial Officer (principal financial officer and principal accounting officer)	February 25, 2016
By:	/s/ Christopher Alafi, Ph.D. Christopher Alafi, Ph.D.	Director	February 25, 2016
By:	/s/ Richard Lerner, M.D. Richard Lerner, M.D.	Director	February 25, 2016
By:	/s/ Joel S. Marcus Joel S. Marcus	Director	February 25, 2016
By:	/s/ Rory B. Riggs Rory B. Riggs	Director	February 25, 2016
By:	/s/ Robert L. Van Nostrand Robert L. Van Nostrand	Director	February 25, 2016



**Table of Contents**

**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders of Intra-Cellular Therapies, Inc.

We have audited the accompanying consolidated balance sheets of Intra-Cellular Therapies, Inc. and subsidiaries as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, stockholders equity and cash flows for each of the three years in the period ended December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Intra-Cellular Therapies, Inc. and subsidiaries at December 31, 2015 and 2014, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Intra-Cellular Therapies, Inc.'s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 25, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Baltimore, MD

February 25, 2016

F-1

**Table of Contents**

Intra-Cellular Therapies, Inc.

Consolidated Balance Sheets

	December 31,	
	2015	2014
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 47,159,303	\$ 61,325,044
Investment securities, available-for-sale	428,041,021	68,320,672
Accounts receivable	30,660	51,603
Prepaid expenses and other current assets	8,025,147	1,288,953
<b>Total current assets</b>	<b>483,256,131</b>	<b>130,986,272</b>
Property and equipment, net	775,522	54,553
Other assets	71,875	70,944
<b>Total assets</b>	<b>\$ 484,103,528</b>	<b>\$ 131,111,769</b>
<b>Liabilities and stockholders equity</b>		
Current liabilities:		
Accounts payable	\$ 1,632,905	\$ 2,052,765
Accrued and other current liabilities	3,423,464	7,529,241
Accrued employee benefits	1,207,143	975,058
<b>Total current liabilities</b>	<b>6,263,512</b>	<b>10,557,064</b>
<b>Long-term deferred rent</b>	<b>1,597,105</b>	
<b>Total liabilities</b>	<b>7,860,617</b>	<b>10,557,064</b>
Stockholders equity:		
Common stock, \$.0001 par value: 100,000,000 shares authorized; 43,155,875 and 29,499,059 shares issued and outstanding at December 31, 2015 and 2014, respectively	4,316	2,950
Additional paid-in capital	669,878,103	208,912,345
Accumulated deficit	(193,049,098)	(88,255,957)
Accumulated comprehensive loss	(590,410)	(104,633)
<b>Total stockholders equity</b>	<b>476,242,911</b>	<b>120,554,705</b>
<b>Total liabilities and stockholders equity</b>	<b>\$ 484,103,528</b>	<b>\$ 131,111,769</b>

*See accompanying notes to consolidated financial statements.*





**Table of Contents**

## Intra-Cellular Therapies, Inc.

## Consolidated Statements of Operations

	Years Ended December 31,		
	2015	2014	2013
<b>Revenues:</b>			
License and collaboration revenue	\$ 30,659	\$ 547,546	\$ 2,737,002
Grant Revenue	60,705	29,755	
Total revenues	91,364	577,301	2,737,002
<b>Costs and expenses:</b>			
Research and development	87,718,074	21,226,345	23,027,578
General and administrative	18,187,286	10,337,679	5,976,276
Total costs and expenses	105,905,360	31,564,024	29,003,854
Loss from operations	(105,813,996)	(30,986,723)	(26,266,852)
Interest income	1,022,455	303,936	29,617
Interest expense		(7,073)	(612,963)
Income tax expense	(1,600)	(1,600)	(18,000)
Net loss	\$ (104,793,141)	\$ (30,691,460)	\$ (26,868,198)
<b>Net loss per common share:</b>			
Basic & Diluted	\$ (2.91)	\$ (1.07)	\$ (1.56)
<b>Weighted average number of common shares:</b>			
Basic & Diluted	36,069,237	28,650,067	17,260,768

*See accompanying notes to consolidated financial statements.*

**Table of Contents**

Intra-Cellular Therapies, Inc.

Consolidated Statements of Comprehensive Loss

	<b>Years Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Net loss	<b>\$ (104,793,141)</b>	\$ (30,691,460)	\$ (26,868,198)
Other comprehensive loss:			
Unrealized loss on investment securities	<b>(485,777)</b>	(104,633)	
Comprehensive loss	<b>\$ (105,278,918)</b>	\$ (30,796,093)	\$ (26,868,198)

*See accompanying notes to consolidated financial statements.*

**Table of Contents**

## Intra-Cellular Therapies, Inc.

## Consolidated Statements of Stockholders' Equity

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2012	14,599,612	1,460	\$ 47,678,924	\$ (30,696,299)	\$	\$ 16,984,085
Conversion of convertible notes	110,446	11	701,712			701,723
Private placement of common stock	6,916,697	692	39,962,808			39,963,500
Exercise of stock options	514,466	51	332,887			332,938
Stock subscription	18,225	2	109,832			109,834
Share-based compensation			391,393			391,393
Net loss				(26,868,198)		(26,868,198)
Balance at December 31, 2013	22,159,446	\$ 2,216	\$ 89,177,556	\$ (57,564,497)	\$	\$ 31,615,275
Common shares issued February 5, 2014	7,063,300	706	115,442,041			115,442,747
Exercise of stock options	247,165	25	162,955			162,980
Stock issued for services	10,923	1	176,084			176,085
Stock subscription	18,225	2	109,831			109,833
Share-based compensation			3,843,878			3,843,878
Net loss				(30,691,460)		(30,691,460)
Other comprehensive loss					(104,633)	(104,633)
Balance at December 31, 2014	29,499,059	\$ 2,950	\$ 208,912,345	\$ (88,255,957)	\$ (104,633)	\$ 120,554,705
Common shares issued March 11, 2015	<b>5,411,481</b>	<b>541</b>	<b>121,803,828</b>			<b>121,804,369</b>
Common shares issued September 28, 2015	<b>7,935,000</b>	<b>793</b>	<b>327,435,412</b>			<b>327,436,205</b>
Exercise of stock options	<b>305,005</b>	<b>31</b>	<b>653,015</b>			<b>653,046</b>
Stock issued for services	<b>5,330</b>	<b>1</b>	<b>182,598</b>			<b>182,599</b>

Share-based compensation				<b>10,890,905</b>				<b>10,890,905</b>
Net loss							<b>(104,793,141)</b>	<b>(104,793,141)</b>
Other comprehensive loss							<b>(485,777)</b>	<b>(485,777)</b>
Balance at December 31, 2015	<b>43,155,875</b>	<b>\$ 4,316</b>	<b>\$ 669,878,103</b>	<b>\$ (193,049,098)</b>	<b>\$ (590,410)</b>			<b>\$ 476,242,911</b>

*See accompanying notes to consolidated financial statements.*

**Table of Contents**

## Intra-Cellular Therapies, Inc.

## Consolidated Statements of Cash Flows

	Years Ended December 31,		
	2015	2014	2013
<b>Operating activities</b>			
Net loss	\$ (104,793,141)	\$ (30,691,460)	\$ (26,868,198)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation expense	139,626	25,481	23,249
Share-based compensation expense	10,890,905	3,843,878	391,393
Issuance of stock for services	182,599	176,085	
Amortization of premiums on investment activities	712,675	297,223	
Changes in operating assets and liabilities:			
Accounts receivable	20,943	284,715	(35,889)
Prepaid expenses and other assets	(6,737,125)	(466,099)	(574,341)
Accounts payable	(419,860)	(1,342,302)	3,353,459
Accrued liabilities and employee benefits	(3,873,692)	5,065,329	2,785,736
Deferred revenue			(1,666,674)
Deferred rent	1,597,105		
Net cash used in operating activities	(102,279,965)	(22,807,150)	(22,591,265)
<b>Investing activities</b>			
Purchases of investments	(514,308,249)	(103,601,836)	
Maturities of investments	153,389,448	36,879,308	1,500,000
Purchase of property and equipment	(860,595)	(11,762)	(33,255)
Net cash (used in) provided by investing activities	(361,779,396)	(66,734,290)	1,466,745
<b>Financing activities</b>			
Proceeds from issuance of convertible promissory notes, net			100,000
Proceeds from stock option exercises	653,046	162,980	332,938
Proceeds from stock subscription		109,833	109,834
Proceeds of public offerings	449,996,887	116,191,285	43,841,850
Payment of costs of public offerings	(756,313)	(748,538)	(3,754,706)
Net cash provided by financing activities	449,893,620	115,715,560	40,629,916
Net (decrease) increase in cash and cash equivalents	(14,165,741)	26,174,120	19,505,396
Cash and cash equivalents at beginning of period	61,325,044	35,150,924	15,645,528
Cash and cash equivalents at end of period	\$ 47,159,303	\$ 61,325,044	\$ 35,150,924
Cash paid for interest	\$	\$ 7,073	\$ 11,320

See accompanying notes to consolidated financial statements.



---

**Table of Contents**

Intra-Cellular Therapies, Inc.

Notes to Consolidated Financial Statements

December 31, 2015

**1. Organization**

Intra-Cellular Therapies, Inc. (the *Company*), through its wholly-owned operating subsidiary, ITI, Inc. (*ITI*), is a biopharmaceutical company focused on the discovery and clinical development of innovative, small molecule drugs that address underserved medical needs in neuropsychiatric and neurological disorders by targeting intracellular signaling mechanisms within the central nervous system (*CNS*). The *Company*'s lead product candidate, ITI-007, is in Phase 3 clinical development as a novel treatment for schizophrenia and bipolar depression.

ITI was incorporated in the State of Delaware on May 22, 2001 under the name *Intra-Cellular Therapies, Inc.* and commenced operations in June 2002. ITI was founded to discover and develop drugs for the treatment of neurological and psychiatric disorders.

On August 29, 2013, ITI completed a reverse merger (the *Merger*) with a public shell company named Oneida Resources Corp. (*Oneida*). Oneida was formed in August 2012 as a vehicle to investigate and, if such investigation warranted, acquire a target company or business seeking the perceived advantages of being a publicly held corporation. In the *Merger*, each outstanding share of capital stock of ITI was exchanged for 0.5 shares of common stock of Oneida, and each outstanding option to purchase one share of ITI common stock and each outstanding warrant to purchase one share of ITI common stock was assumed by Oneida and became exercisable for 0.5 shares of Oneida common stock. As a result of the *Merger* and related transactions, ITI survived as a wholly-owned subsidiary of Oneida, Oneida changed its fiscal year end from March 31 to December 31, and Oneida changed its name to *Intra-Cellular Therapies, Inc.* (the *Company*). In addition, the *Company* began operating ITI and its business, and therefore ceased being a shell company. Following the *Merger* and the redemption of all then outstanding shares of Oneida at the closing of the *Merger*, the former stockholders of ITI owned 100% of the shares of the *Company*'s outstanding capital stock.

In accordance with Financial Accounting Standards Board (*FASB*), Accounting Standards Codification (*ASC*) Topic 805, *Business Combinations*, ITI is considered the acquirer for accounting purposes, and has accounted for the transaction as a capital transaction, because ITI's former stockholders received 100% of the voting rights in the combined entity and ITI's senior management represented all of the senior management of the combined entity. Consequently, the assets and liabilities and the historical operations that are reflected in the *Company*'s consolidated financial statements are those of ITI and have been recorded at the historical cost basis of the *Company*. All share and per share amounts in the consolidated financial statements and related notes have been retrospectively adjusted to reflect the one-for-0.5 shares of capital stock exchange as well as the conversion of the Notes (defined below) and the Series A, B, and C redeemable convertible preferred stock of ITI.

Immediately prior to the *Merger*, on August 29, 2013, ITI sold to accredited investors approximately \$60.0 million of its shares of common stock, or 18,889,307 shares at a price of \$3.1764 per share (the *Private Placement*), which included \$15.3 million in principal and \$0.8 million in accrued interest from the conversion of ITI's then outstanding convertible promissory notes (the *Notes*).

On February 5, 2014, the *Company* completed a public offering of common stock in which the *Company* sold 7,063,300 shares of common stock, which included the exercise of the underwriters' option to purchase an additional



921,300 shares, at an offering price of \$17.50 per share. After deducting underwriting discounts, commissions and offering expenses, the net proceeds to the Company were approximately \$115.4 million.

F-7

## **Table of Contents**

### **1. Organization (continued)**

On October 31, 2014, the Company entered into a termination agreement with Takeda Pharmaceutical Company Limited ( Takeda ) terminating the worldwide license and collaboration agreement under which the Company and Takeda were jointly developing the Company s proprietary compound ITI-214 and other selected compounds that selectively inhibit phosphodiesterase type 1 ( PDE1 ) for use in the prevention and treatment of human diseases. Through December 31, 2015, the Company had received \$29.0 million in total payments under the agreement and was eligible to receive milestone payments and royalties based on net sales. On September 15, 2015, Takeda completed the transfer of the Investigational New Drug application ( IND ) for ITI-214 to the Company. The Company intends to explore the development of its PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions.

On March 11, 2015, the Company completed a public offering of common stock in which the Company sold 5,411,481 shares of common stock, which included the exercise of the underwriters option to purchase an additional 661,481 shares, at an offering price of \$24.00 per share. After deducting underwriting discounts, commissions and offering expenses, the net proceeds to the Company were approximately \$121.8 million.

On September 28, 2015, the Company completed a public offering of common stock in which the Company sold 7,935,000 shares of common stock, which included the exercise of the underwriters option to purchase an additional 1,035,000 shares, at an offering price of \$43.50 per share. After deducting underwriting discounts, commissions and offering expenses, the net proceeds to the Company were approximately \$327.4 million.

In order to further its research projects and support its collaborations, the Company will require additional financing until such time, if ever, that revenue streams are sufficient to generate consistent positive cash flow from operations. Possible sources of funds include public or private sales of the Company s equity securities, sales of debt securities, the incurrence of debt from commercial lenders, strategic collaborations, licensing a portion or all of the Company s product candidates and technology and, to a lesser extent, grant funding.

### **2. Summary of Significant Accounting Policies**

#### **Basis of Presentation**

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ( GAAP ). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ( ASC ) and Accounting Standards Update ( ASU ) of the Financial Accounting Standards Board ( FASB ).

#### **Use of Estimates**

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Although actual results could differ from those estimates, management does not believe that such differences would be material.

#### **Cash and Cash Equivalents**

The Company considers all highly liquid investments with a maturity of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents consist of checking accounts, money market accounts, money market mutual funds, and certificates of deposit with a maturity date of three months or less. Their carrying values approximate the fair market value. Certificates of deposit, commercial paper, corporate notes and corporate bonds with a maturity date of more than three months are classified separately on the balance sheet.

F-8

**Table of Contents****2. Summary of Significant Accounting Policies (continued)****Investment Securities**

Investment securities may consist of investments in U.S. Treasuries, various U.S. governmental agency debt securities, corporate bonds, certificates of deposit, and other fixed income securities with an average maturity of twelve months or less. Management classifies the Company's investments as available-for-sale. Such securities are carried at estimated fair value, with any unrealized holding gains or losses reported, net of any tax effects reported, as accumulated other comprehensive income, which is a separate component of stockholders' equity. Realized gains and losses, and declines in value judged to be other-than-temporary, if any, are included in consolidated results of operations. A decline in the market value of any available-for-sale security below cost that is deemed to be other-than-temporary results in a reduction in fair value, which is charged to earnings in that period, and a new cost basis for the security is established. Dividend and interest income is recognized as interest income when earned. The cost of securities sold is calculated using the specific identification method.

Investment securities consisted of the following (in thousands):

	<b>December 31, 2015</b>			<b>Estimated Fair Value</b>
	<b>Amortized Cost</b>	<b>Unrealized Gains</b>	<b>Unrealized (Losses)</b>	
U.S. government agency securities	\$ 61,510	\$	\$ (271)	\$ 61,239
FDIC certificates of deposit (1)	41,343	1	(11)	41,333
Certificates of deposit	219,500			219,500
Commercial paper	30,122		(48)	30,074
Corporate bonds/notes	76,157		(262)	75,895
	\$ 428,632	\$ 1	\$ (592)	\$ 428,041

	<b>December 31, 2014</b>			<b>Estimated Fair Value</b>
	<b>Amortized Cost</b>	<b>Unrealized Gains</b>	<b>Unrealized (Losses)</b>	
U.S. government agency securities	\$ 4,316	\$	\$ (3)	\$ 4,313
FDIC certificates of deposit (1)	16,374		(14)	16,360
Certificates of deposit	2,000			2,000
Commercial paper	9,743	1		9,744
Corporate bonds/notes	35,992		(89)	35,904
	\$ 68,425	\$ 1	\$ (106)	\$ 68,321

(1) FDIC certificates of deposit consist of deposits that are less than \$250,000.

The Company has classified all of its investment securities available-for-sale, including those with maturities beyond one year, as current assets on the consolidated balance sheets based on the highly liquid nature of the investment securities and because these investment securities are considered available for use in current operations. As of December 31, 2015 and December 31, 2014, the Company held \$142.4 million and \$31.8 million, respectively, of available-for-sale investment securities with contractual maturity dates more than one year and less than two years.

The Company monitors its investment portfolio for impairment quarterly or more frequently if circumstances warrant. In the event that the carrying value of an investment exceeds its fair value and the decline in value is determined to be other-than-temporary, the Company records an impairment charge within earnings attributable to the estimated credit loss. In determining whether a decline in the value of an investment is other-than-temporary, the Company evaluates currently available factors that may include, among others: (1) general market conditions; (2) the duration and extent to which fair value has been less than the carrying

**Table of Contents**

**2. Summary of Significant Accounting Policies (Continued)**

value; (3) the investment issuer's financial condition and business outlook; and (4) our assessment as to whether it is more likely than not that we will be required to sell a security prior to recovery of its amortized cost basis.

As of December 31, 2015 the Company had approximately \$9.2 million of investments that have been held for greater than one year which had a temporary impairment of approximately \$19,000. As of December 31, 2014 the Company had no investments that had been held for greater than one year.

The Company attributes the unrealized losses on the available-for-sale securities as of December 31, 2015 and 2014, to the variability in related market interest rates. The Company does not intend to sell these securities, nor is it more likely than not that the Company will be required to sell them prior to the end of their contractual terms. Furthermore, the Company does not believe that these securities expose us to undue market risk or counterparty credit risk. As such, the Company does not consider these securities to be other-than-temporarily impaired.

**Fair Value Measurements**

The Company applies the fair value method under ASC Topic 820, *Fair Value Measurements and Disclosures*. ASC Topic 820 defines fair value, establishes a fair value hierarchy for assets and liabilities measured at fair value and requires expanded disclosures about fair value measurements. The ASC Topic 820 hierarchy ranks the quality and reliability of inputs, or assumptions, used in the determination of fair value and requires assets and liabilities carried at fair value to be classified and disclosed in one of the following categories based on the lowest level input used that is significant to a particular fair value measurement:

Level 1 Fair value is determined by using unadjusted quoted prices that are available in active markets for identical assets and liabilities.

Level 2 Fair value is determined by using inputs other than Level 1 quoted prices that are directly or indirectly observable. Inputs can include quoted prices for similar assets and liabilities in active markets or quoted prices for identical assets and liabilities in inactive markets. Related inputs can also include those used in valuation or other pricing models, such as interest rates and yield curves that can be corroborated by observable market data.

Level 3 Fair value is determined by inputs that are unobservable and not corroborated by market data. Use of these inputs involves significant and subjective judgments to be made by a reporting entity e.g., determining an appropriate adjustment to a discount factor for illiquidity associated with a given security.

The Company evaluates financial assets and liabilities subject to fair value measurements on a recurring basis to determine the appropriate level at which to classify them each reporting period. This determination requires the Company to make subjective judgments as to the significance of inputs used in determining fair value and where such inputs lie within the ASC Topic 820 hierarchy.

The Company has no assets or liabilities that were measured using quoted prices for significant unobservable inputs (Level 3 assets and liabilities) as of December 31, 2015 and December 31, 2014. The carrying value of cash held in money market funds of approximately \$31.1 million as of December 31, 2015 and \$8.5 million as of December 31, 2014, is included in cash and cash equivalents and approximates market value based on quoted market price or Level 1 inputs.

F-10

**Table of Contents****2. Summary of Significant Accounting Policies (continued)**

The fair value measurements of the Company's cash equivalents and available-for-sale investment securities are identified in the following tables (in thousands):

	<b>Fair Value Measurements at Reporting Date Using</b>			
	<b>Quoted Prices in Active Markets for Identical Assets (Level 1)</b>			
	<b>December 31, 2015</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>	
Money market funds	\$ 31,114	\$ 31,114	\$	\$
U.S. government agency securities	61,239		61,239	
FDIC certificates of deposit	41,333		41,333	
Certificates of deposit	219,500		219,500	
Commercial paper	30,074		30,074	
Corporate bonds/notes	75,895		75,895	
	<b>\$ 459,155</b>	<b>\$ 31,114</b>	<b>\$ 428,041</b>	<b>\$</b>

	<b>Fair Value Measurements at Reporting Date Using</b>			
	<b>Quoted Prices in Active Markets for Identical Assets (Level 1)</b>			
	<b>December 31, 2014</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>	
Money market funds	\$ 8,495	\$ 8,495	\$	\$
U.S. government agency securities	4,313		4,313	
FDIC certificates of deposit	16,360		16,360	
Certificates of deposit	41,000		41,000	
Commercial paper	9,744		9,744	
Corporate bonds/notes	35,903		35,903	



\$	115,815	\$	8,495	\$	107,320	\$
----	---------	----	-------	----	---------	----

**Financial Instruments**

The Company considers the recorded costs of its financial assets and liabilities, which consist of cash equivalents, accounts receivable, accounts payable and accrued liabilities, to approximate their fair value because of their relatively short maturities at December 31, 2015 and December 31, 2014. Management believes that the risks associated with its financial instruments are minimal as the counterparties are various corporations, financial institutions and government agencies of high credit standing.

**Concentration of Credit Risk**

Cash equivalents are held with major financial institutions in the United States. Certificates of deposit, cash and cash equivalents held with banks may exceed the amount of insurance provided on such deposits. Generally, these deposits may be redeemed upon demand and, therefore, bear minimal risk.

**Accounts Receivable**

Accounts receivable that management has the intent and ability to collect are reported in the balance sheets at outstanding amounts, less an allowance for doubtful accounts. The Company writes off uncollectible receivables when the likelihood of collection is remote.

---

**Table of Contents****2. Summary of Significant Accounting Policies (continued)**

The Company evaluates the collectability of accounts receivable on a regular basis. The allowance, if any, is based upon various factors including the financial condition and payment history of customers, an overall review of collections experience on other accounts and economic factors or events expected to affect future collections experience. No allowance was recorded as of December 31, 2015 and 2014, as the Company has a history of collecting on all its accounts including government agencies and collaborations funding its research.

**Property and Equipment**

Property and equipment is stated at cost and depreciated on a straight-line basis over estimated useful lives ranging from three to five years. Leasehold improvements are amortized using the straight-line method over the shorter of the estimated useful life of the assets or the term of the related lease. Expenditures for maintenance and repairs are charged to operations as incurred.

When indicators of possible impairment are identified, the Company evaluates the recoverability of the carrying value of its long-lived assets based on the criteria established in ASC 360, *Property, Plant and Equipment*. The Company considers historical performance and anticipated future results in its evaluation of potential impairment. The Company evaluates the carrying value of those assets in relation to the operating performance of the business and undiscounted cash flows expected to result from the use of those assets. Impairment losses are recognized when carrying value exceeds the undiscounted cash flows, in which case management must determine the fair value of the underlying asset. No such impairment losses have been recognized to date.

**Revenue Recognition**

Revenue is recognized when all terms and conditions of the agreements have been met, including persuasive evidence of an arrangement, delivery has occurred or services have been rendered, price is fixed or determinable and collectability is reasonably assured. The Company is reimbursed for certain costs incurred on specified research projects under the terms and conditions of grants, collaboration agreements, and awards. The Company records the amount of reimbursement as revenues on a gross basis in accordance with ASC Topic 605-45, *Revenue Recognition/Principal Agent Considerations*. The Company is the primary obligor with respect to purchasing goods and services from third-party suppliers, is obligated to compensate the service provider for the work performed, and has discretion in selecting the supplier. Provisions for estimated losses on research grant projects and any other contracts are made in the period such losses are determined.

The Company has entered into arrangements involving the delivery of more than one element. Each required deliverable is evaluated to determine whether it qualifies as a separate unit of accounting. For the Company, this determination is generally based on whether the deliverable has stand-alone value to the customer. The Company adopted this accounting standard on a prospective basis for all Multiple-Deliverable Revenue Arrangements ( MDRAs ) entered into on or after January 1, 2011, and for any MDRAs that were entered into prior to January 1, 2011, but materially modified on or after that date.

The Company has adopted ASC Topic 605-28, *Milestone Method*. Under this guidance, the Company recognizes revenue contingent upon the achievement of a substantive milestone in its entirety in the period the milestone is achieved. Substantive milestone payments are recognized upon achievement of the milestone only if all of the following conditions are met:

The milestone payments are non-refundable;

Achievement of the milestone involves a degree of risk and was not reasonably assured at the inception of the arrangement;

Substantive effort on the Company's part is involved in achieving the milestone;

The amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and

F-12

---

**Table of Contents****2. Summary of Significant Accounting Policies (continued)**

A reasonable amount of time passes between the up-front license payment and the first milestone payment, as well as between each subsequent milestone payment.

Determination as to whether a payment meets the aforementioned conditions involves management's judgment. If any of these conditions are not met, the resulting payment would not be considered a substantive milestone, and therefore, the resulting payment would be considered part of the consideration for the single unit of accounting and be recognized as revenue in accordance with the revenue models described above. In addition, the determination that one such payment was not a substantive milestone could prevent the Company from concluding that subsequent milestone payments were substantive milestones and, as a result, any additional milestone payments could also be considered part of the consideration for the single unit of accounting and would be recognized as revenue as such performance obligations are performed under either the proportional performance or straight-line methods, as applicable.

**Research and Development**

Except for payments made in advance of services, the Company expenses its research and development costs as incurred. For payments made in advance, the Company recognizes research and development expense as the services are rendered. Research and development costs primarily consist of salaries and related expenses for personnel and resources and the costs of clinical trials. Other research and development expenses include preclinical analytical testing, outside services, providers, materials and consulting fees.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to the Company by its vendors with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

As part of the process of preparing its financial statements, the Company is required to estimate its expenses resulting from its obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company's objective is to reflect the appropriate trial expenses in its financial statements by matching those expenses with the period in which services are performed and efforts are expended. The Company accounts for these expenses according to the progress of the trial as measured by subject progression and the timing of various aspects of the trial. The Company determines accrual estimates through financial models taking into account discussion with applicable personnel and outside service providers as to the progress or state of consummation of trials, or the services completed. During the course of a clinical trial, the Company adjusts its clinical expense recognition if actual results differ from its estimates. The Company makes estimates of its accrued expenses as of each balance sheet date based on the facts and circumstances known to it at that time. The Company's clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in it reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2015 and 2014, there were no material adjustments to the Company's prior period estimates of accrued expenses for clinical trials.

**Income Taxes**

Income taxes are accounted for using the liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of

F-13

---

**Table of Contents****2. Summary of Significant Accounting Policies (continued)**

existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the year in which those temporary differences are expected to be recovered or settled.

The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Valuation allowances are established when necessary to reduce net deferred tax assets to the amount expected to be realized. Income tax expense is the tax payable for the period and the change during the period in deferred tax assets and liabilities.

The Company accounts for uncertain tax positions pursuant to ASC Topic 740 (previously included in FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes – an Interpretation of FASB Statement No. 109*). Financial statement recognition of a tax position taken or expected to be taken in a tax return is determined based on a more-likely-than-not threshold of that position being sustained. If the tax position meets this threshold, the benefit to be recognized is measured as the tax benefit having the highest likelihood of being realized upon ultimate settlement with the taxing authority. The Company recognizes interest accrued related to unrecognized tax benefits and penalties in the provision for income taxes.

**Comprehensive Income (Loss)**

All components of comprehensive income (loss), including net income (loss), are reported in the financial statements in the period in which they are incurred. Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. In accordance with accounting guidance, the Company presents the impact of any unrealized gains or (losses) on its investment securities in a separate statement of comprehensive income (loss) for each period.

**Share-Based Compensation**

Share-based payments are accounted for in accordance with the provisions of ASC Topic 718, *Compensation – Stock Compensation*. The fair value of share-based payments is estimated, on the date of grant, using the Black-Scholes-Merton option-pricing model (the Black-Scholes model). The resulting fair value is recognized ratably over the requisite service period, which is generally the vesting period of the option.

For all awards granted with time-based vesting conditions, expense is amortized using the straight-line attribution method. For awards that contain a performance-based vesting condition, expense is amortized using the accelerated attribution method. Share-based compensation expense recognized in the statements of operations for the years ended December 31, 2015, 2014 and 2013 is based on share-based awards ultimately expected to vest, and this amount has therefore been reduced for estimated forfeitures. ASC Topic 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Pre-vesting forfeitures were estimated based on the Company's historical experience and have not been material.

The Company utilizes the Black-Scholes model for estimating fair value of its stock options granted. Option valuation models, including the Black-Scholes model, require the input of subjective assumptions, and changes in the assumptions used can materially affect the grant date fair value of an award. These assumptions include the risk-free rate of interest, expected dividend yield, expected volatility and the expected life of the award. Restricted stock units

are valued at the fair market value on the date of grant as determined by the closing stock price.

Expected volatility rates are based on historical volatility of the common stock of comparable publicly traded entities and other factors due to the limited historical information about the Company's common stock. The expected life of stock options is the period of time for which the stock options are expected to be outstanding.

**Table of Contents**

**2. Summary of Significant Accounting Policies (continued)**

Given the limited historical exercise data, the expected life is determined using the simplified method, which is defined as the midpoint between the vesting date and the end of the contractual term.

The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. The Company has not paid dividends to its stockholders since its inception and does not plan to pay cash dividends in the foreseeable future. Therefore, the Company has assumed an expected dividend rate of zero.

Prior to January 1, 2014, given that there was no active market for the Company's common stock, the exercise price of the stock options on the date of grant was determined and approved by the board of directors using several factors, including progress and milestones achieved in the Company's business development and performance, the price per share of its convertible preferred stock offerings and general industry and economic trends. In establishing the estimated fair value of the common stock, the Company considered the guidance set forth in American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. For stock options granted in 2014 and 2015, the exercise price was determined by using the closing market price of the Company's common stock on the date of grant.

Under ASC Topic 718, the cumulative amount of compensation cost recognized for instruments classified as equity that ordinarily would result in a future tax deduction under existing tax law shall be considered to be a deductible temporary difference in applying ASC Topic 740, *Income Taxes*. The deductible temporary difference is based on the compensation cost recognized for financial reporting purposes; however, these provisions currently do not impact the Company, as all the deferred tax assets have a full valuation allowance.

Since the Company had net operating loss carryforwards as of December 31, 2015, 2014 and 2013, no excess tax benefits for the tax deductions related to share-based awards were recognized in the statements of operations.

Equity instruments issued to consultants are accounted for under the provisions of ASC Topic 718 and ASC Topic 505-50, *Equity/Equity-Based Payments to Non-Employees*. Accordingly, the estimated fair value of the equity instrument is recorded on the earlier of the performance commitment date or the date the services required are completed and are marked to market during the service period.

**Loss Per Share**

Basic net loss per common share is determined by dividing the net loss by the weighted-average number of common shares outstanding during the period, without consideration of common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of common stock equivalents outstanding for the period. The treasury stock method is used to determine the dilutive effect of the Company's stock option grants.

The following common stock equivalents were excluded in the calculation of diluted loss per share because their effect would be anti-dilutive as applied to the loss from operations for the years ended December 31, 2015, 2014 and 2013:



	<b>Years Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Stock Equivalents	1,322,311	958,712	898,982

**Recently Issued Accounting Standards**

In November 2015, the FASB issued Accounting Standards Update No. 2015-17, Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes. Current GAAP requires an entity to separate deferred income tax liabilities and assets into current and noncurrent amounts in a classified statement of financial position. To simplify the presentation of deferred income taxes, ASU 2015-17 requires that deferred tax

**Table of Contents****2. Summary of Significant Accounting Policies (continued)**

liabilities and assets be classified as noncurrent in a classified statement of financial position. The current requirement that deferred tax liabilities and assets of a tax-paying component of an entity be offset and presented as a single amount is not affected by the amendments in this Update. The amendments in this Update are effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Earlier application is permitted for all entities as of the beginning of an interim or annual reporting period. The Company has elected to adopt this update as of the fourth quarter of 2015, retrospectively. The adoption of this standard did not have a material impact on the Company's consolidated financial statements and accompanying notes.

In May 2014, the FASB issued Accounting Standards Update No. 2014-09 (ASU 2014-09), Revenue from Contracts with Customers. ASU 2014-09 will eliminate transaction-specific and industry-specific revenue recognition guidance under current GAAP and replace it with a principle-based approach for determining revenue recognition. ASU 2014-09 will require that companies recognize revenue based on the value of transferred goods or services as they occur in the contract. ASU 2014-09 also will require additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. In July 2015, the FASB decided to defer the effective date of the standard from January 1, 2017, to January 1, 2018, with an option that permits companies to adopt the standard as early as the original effective date. Early application prior to the original effective date is not permitted. The standard permits the use of either the retrospective or cumulative effect transition method. Presently, the Company is assessing what effect the adoption of this standard will have on our consolidated financial statements and accompanying notes.

**3. Property and Equipment**

Property and equipment consist of the following:

	<b>December 31,</b>	
	<b>2015</b>	<b>2014</b>
Computer equipment	\$ 42,064	\$ 39,160
Furniture and fixtures	266,695	35,958
Scientific equipment	2,823,601	2,207,848
	3,132,360	2,282,966
Less accumulated depreciation	(2,356,838)	(2,228,413)
	\$ 775,522	\$ 54,553

Depreciation expense for the years ended December 31, 2015, 2014 and 2013 was \$139,626, \$25,481 and \$23,249, respectively. During 2015, the Company retired \$11,201 of fully depreciated property and equipment. During 2014, in conjunction with its move in February 2015 to its new headquarters, the Company retired \$319,553 of fully depreciated leasehold improvements and disposed of \$709,518 of fully depreciated property and equipment.

**4. Share-Based Compensation**

Edgar Filing: Intra-Cellular Therapies, Inc. - Form 10-K

The Company sponsors the Intra-Cellular Therapies, Inc. 2013 Equity Incentive Plan (the 2013 Plan ) to provide for the granting of stock-based awards, such as stock options, restricted common stock, restricted stock units and stock appreciation rights to employees, directors and consultants as determined by the Board of Directors. In August 2013, the Company assumed in the Merger the ITI 2003 Equity Incentive Plan, as amended (the 2003 Plan ), which expired by its terms in July 2013. As of December 31, 2015, there were options to

F-16

**Table of Contents****4. Share-Based Compensation (continued)**

purchase 2,737,657 shares of common stock outstanding under the 2013 Plan. Effective in November 2013, the Company adopted the 2013 Plan. The Company initially reserved 2,850,000 shares of common stock for issuance under the 2013 Plan. In both January 2015 and 2014, the number of shares of common stock reserved for issuance under the 2013 Plan automatically increased by 800,000 pursuant to the evergreen provisions of the 2013 Plan. On June 16, 2015, the stockholders of the Company approved, at the Company's 2015 Annual Meeting of Stockholders, an amendment to the 2013 Plan to increase the number of shares of common stock available for issuance under the plan by 3,100,000 shares, to increase by 100,000 shares the maximum number of shares available for the issuance of options, stock appreciation rights and other similar awards to any one participant in any calendar year for purposes of meeting the requirements for qualified performance-based compensation under Section 162(m) of the Internal Revenue Code of 1986, as amended (the Code), and to eliminate the evergreen provisions of the 2013 Plan under which 800,000 shares were automatically added to the plan on each of January 1, 2014 and 2015.

Stock options granted under the 2013 Plan may be either incentive stock options (ISOs) as defined by the Code, or non-qualified stock options. The Board of Directors determines who will receive options, the vesting periods (which are generally two to three years) and the exercise prices of such options. Options have a maximum term of 10 years. The exercise price of ISOs granted under the 2013 Plan must be at least equal to the fair market value of the common stock on the date of grant.

Total stock-based compensation expense related to all of the Company's share-based awards, including stock options and restricted stock units to employees, directors and consultants recognized during the years ended December 31, 2015, 2014 and 2013, was comprised of the following:

	<b>Years Ended December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Research and development	<b>\$ 4,768,131</b>	\$ 1,842,828	\$ 132,543
General and administrative	<b>6,122,774</b>	2,001,050	258,850
<b>Total share-based compensation expense</b>	<b>\$ 10,890,905</b>	\$ 3,843,878	\$ 391,393

The following table describes the weighted-average assumptions used for calculating the value of options granted during the years ended December 31, 2015, 2014 and 2013:

	<b>2015</b>	<b>2014</b>	<b>2013</b>
Dividend yield	<b>0%</b>	0%	0%
Expected volatility	<b>80.0%</b>	80.0%	80.0%
Weighted-average risk-free interest rate	<b>1.8%</b>	2.0%	2.2%
Expected term (in years)	<b>5.9</b>	6.3	6.2

Information regarding the stock options activity, including with respect to grants to employees, directors and consultants as of December 31, 2015, and changes during the period then ended, are summarized as follows:

	<b>Number of Shares</b>	<b>Weighted- Average Exercise Price</b>	<b>Aggregate Intrinsic Value</b>	<b>Weighted- Average Contractual Life</b>
Outstanding at December 31, 2014	2,233,460	\$ 9.20	\$	7.3 years
Options granted	884,703	\$ 21.00	\$	9.1 years
Options exercised	(305,005)	\$ 2.14	\$	2.2 years
Options canceled or expired	(75,501)	\$ 12.33	\$	8.0 years
Outstanding at December 31, 2015	2,737,657	\$ 13.72	\$ 109,778,658	7.6 years
Vested or expected to vest at December 31, 2015	2,737,657	\$ 13.72	\$	
Exercisable at December 31, 2015	1,485,918	\$ 8.75	\$ 66,920,372	6.7 years

F-17

**Table of Contents****4. Share-Based Compensation (continued)**

The weighted-average grant date fair value for awards granted during the years ended December 31, 2015, 2014, and 2013, was \$21.00, \$16.50, and \$3.26 per share, respectively. Total intrinsic value of the options exercised during the years ended December 31, 2015, 2014, and 2013 was approximately \$10,951,057, \$3,696,775 and \$580,623, respectively. The total fair value of shares vested in the years ended December 31, 2015, 2014 and 2013, was approximately \$5,207,073, \$3,703,000 and \$278,000, respectively.

During 2015, 2014 and 2013, the Company granted options to certain scientific advisory board members of the Company to purchase 45,571, 95,000 and 19,000 shares of common stock at an average exercise price per share of \$17.57, \$16.86, and \$3.26, respectively. The options vest ratably over a period of 12 to 24 months. Stock compensation related to these grants will fluctuate with any changes in the underlying value of the Company's common stock, as the performance period is not fixed.

The unrecognized share-based compensation expense related to stock option awards at December 31, 2015, is \$12,733,859 and will be recognized over a weighted-average period of 1.6 years.

**5. Income Taxes**

Total income tax expense for the years ended December 31 is allocated as follows:

	<b>December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Current	\$ 1,600	\$ 1,600	\$ 18,000
Deferred	(51,165,859)	(14,655,320)	(13,229,355)
Valuation allowance	51,165,859	14,655,320	13,229,355
Provision for income taxes	\$ 1,600	\$ 1,600	\$ 18,000

A reconciliation of the difference between the statutory federal income tax rate and the effective income tax rate for the years ended December 31 is as follows:

	<b>December 31,</b>		
	<b>2015</b>	<b>2014</b>	<b>2013</b>
Income tax benefit at statutory federal rate	35.00%	35.00%	35.00%
Permanent differences	(0.56)	0.12	(1.20)
Return-to-provision R&D Credit	0.00	(0.05)	2.61
R&D Credit current year	4.19	2.32	3.72
Reserve for uncertain tax positions	0.00	(0.01)	(6.53)
Change in effective state tax rates	(0.05)	(0.14)	6.58
State income tax expense	10.24	10.50	10.12
Change in valuation allowance	(48.82)	(47.75)	(50.37)

Provision for income taxes	(0.00)%	(0.01)%	(0.07)%
----------------------------	---------	---------	---------

Deferred income taxes reflect the net tax effect of temporary differences that exist between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, using enacted tax rates in effect for the year in which the differences are expected to reverse. As of December 31, 2015, the Company had \$174.8 million of federal net operating loss carryforwards, which expire at various dates through 2035. The gross amount of the state net operating loss carryforwards is equal to or less than the federal net operating loss carryforwards and expires over various periods based on individual state tax law. In general, businesses with U.S. net operating losses ( NOLs ) are considered loss corporations for U.S. federal income tax purposes. Pursuant to Section 382 of the Code, loss corporations that undergo an ownership change, as defined under the Code, may be subject to an annual limitation on the amount of NOLs (and certain other tax attributes)

**Table of Contents****5. Income Taxes (continued)**

available to offset taxable income earned after such ownership change. For the year ended December 31, 2015, the Company performed a Section 382 ownership analysis and determined that an ownership change occurred (within the meaning of Section 382 of the Code) in 2015. Based on the analysis performed, however, the Company does not believe that the Section 382 annual limitation will impact the Company's ability to utilize the tax attributes that existed as of the date of the ownership change in a material manner. If the Company experiences an ownership change in the future, the tax benefits related to the NOLs and tax credit carryforwards may be further limited or lost.

At December 31, 2015, the Company had \$5.7 million in excess tax benefits related to stock-based compensation deductions, the benefit of which will be recorded to additional paid-in-capital once the benefit is realized through a reduction of income taxes payable. The following summarizes the significant components of the Company's deferred tax assets and liabilities as of December 31, 2015 and 2014, respectively:

	<b>December 31,</b>	
	<b>2015</b>	<b>2014</b>
<b>Deferred tax assets:</b>		
Net operating loss carryforwards	\$ 76,741,198	\$ 34,870,169
Accrued employee benefits	543,466	443,371
Research and development credit	6,962,731	2,570,540
Stock compensation	5,641,993	1,563,785
Deferred rent	725,195	
<b>Deferred tax liabilities:</b>		
Depreciation	(6,062)	(5,204)
<b>Net deferred tax asset</b>	<b>90,608,521</b>	<b>39,442,661</b>
Valuation allowance	(90,608,521)	(39,442,661)
<b>Net deferred tax asset</b>	<b>\$</b>	<b>\$</b>

Based upon the Company's historical operating performance and the reported cumulative net losses to date, the Company presently does not have sufficient objective evidence to support the recovery of its net deferred tax assets. Accordingly, the Company has established a valuation allowance against its net deferred tax assets for financial reporting purposes because it is not more likely than not that these deferred tax assets will be realized.

The total amount of unrecognized tax benefits as of December 31, 2015 and December 31, 2014 were \$1.72 million and \$1.72 million respectively. If recognized none of these tax benefits would affect the effective tax rate due to valuation allowances.

The following summarizes the significant components of gross unrecognized tax benefits as of December 31, 2015 and 2014, respectively:



	<b>December 31,</b>	
	<b>2015</b>	<b>2014</b>
Balance at January 1,	<b>\$ 1,717,635</b>	\$ 1,715,904
Current Year Uncertain Tax Positions:		
Gross Increases	3,277	1,731
Prior Year Uncertain Tax Positions:		
Balance at December 31,	<b>\$ 1,720,912</b>	\$ 1,717,635

F-19

---

**Table of Contents****6. Collaborations and License Agreements***The Bristol-Myers Squibb License Agreement*

On May 31, 2005, the Company entered into a worldwide, exclusive License Agreement with Bristol-Myers Squibb Company ( BMS ), pursuant to which the Company holds a license to certain patents and know-how of BMS relating to ITI-007 and other specified compounds. The agreement was amended on November 3, 2010. The licensed rights are exclusive, except BMS retains rights in specified compounds in the fields of obesity, diabetes, metabolic syndrome and cardiovascular disease. However, BMS has no right to use, develop or commercialize ITI-007 and other specified compounds in any field of use. The Company has the right to grant sublicenses of the rights conveyed by BMS. The Company is obliged under the license to use commercially reasonable efforts to develop and commercialize the licensed technology. The Company is also prohibited from engaging in the clinical development or commercialization of specified competitive compounds.

Under the agreement, the Company made an upfront payment of \$1.0 million to BMS, a milestone payment of \$1.25 million in December 2013, and a milestone payment of \$1.5 million in December 2014 following the initiation of the Company's first Phase 3 clinical trial for ITI-007 for patients with exacerbated schizophrenia. Possible milestone payments remaining total \$12.0 million. Under the agreement, the Company may be obliged to make other milestone payments to BMS for each licensed product of up to an aggregate of approximately \$14.75 million. The Company is also obliged to make tiered single digit percentage royalty payments on sales of licensed products. The Company is obliged to pay to BMS a percentage of non-royalty payments made in consideration of any sublicense.

The agreement extends, and royalties are payable, on a country-by-country and product-by-product basis, through the later of ten years after first commercial sale of a licensed product in such country, expiration of the last licensed patent covering a licensed product, its method of manufacture or use, or the expiration of other government grants providing market exclusivity, subject to certain rights of the parties to terminate the agreement on the occurrence of certain events. On termination of the agreement, the Company may be obliged to convey to BMS rights in developments relating to a licensed compound or licensed product, including regulatory filings, research results and other intellectual property rights.

*The Takeda Pharmaceutical License and Collaboration Agreement and Termination Agreement*

On February 25, 2011, the Company entered into a license and collaboration agreement with Takeda Pharmaceutical Company Limited under which the Company agreed to collaborate to research, develop and commercialize its proprietary compound ITI-214 and other selected compounds that selectively inhibit PDE1 for use in the prevention and treatment of human diseases. As part of the agreement, the Company assigned to Takeda certain patents owned by the Company that claim ITI-214 and granted Takeda an exclusive license to develop and commercialize compounds identified in the conduct of the research program that satisfy specified criteria. However, the Company retained rights to all compounds that do not meet the specified criteria and the Company continues to develop PDE1 inhibitors outside the scope of the agreement.

Under the terms of the agreement, the Company conducted a research program with an initial term of three years to identify and characterize compounds that meet certain specified criteria sufficient for further development by Takeda. This research program ended in February 2014. The Company was responsible for its expenses incurred in the conduct of certain research activities specified in the research plan. Takeda agreed to reimburse the Company for expenses the Company incurred in conducting additional research activities.

Upon execution of the agreement, Takeda made a nonrefundable payment to the Company. The Company was eligible to receive payments of approximately \$500 million in the aggregate upon achievement of certain development milestones and up to an additional \$250 million in the aggregate upon achievement of certain sales-based milestones, along with tiered royalty payments ranging from the high single digits to the low teens in percent based on net sales by Takeda.

F-20

**Table of Contents****6. Collaborations and License Agreements (continued)**

On October 31, 2014, the Company entered into an agreement with Takeda terminating the Takeda License Agreement, pursuant to which all rights granted under the Takeda License Agreement were returned to the Company. On September 15, 2015, Takeda completed the transfer of the IND for ITI-214 to the Company. ITI-214 is the first compound in its class to successfully advance into Phase 1 clinical trials. The Company intends to explore the development of its PDE program, including ITI-214 for the treatment of several CNS and non-CNS conditions, which may include cognition in Parkinson's disease, cognition in Alzheimer's disease, cognition in schizophrenia and in other non-CNS indications. Other compounds in the PDE portfolio are also being advanced for the treatment of various indications.

**Other License Agreement**

In May 2002, ITI entered into a license agreement (the "License") and research agreement with a university. Under the provisions of the License, ITI is entitled to use this organization's patented technology and other intellectual property relating to diagnosis and treatment of central nervous system disorders.

The License expires upon expiration of the patent rights or 15 years subsequent to the first sale of products developed through this License. ITI is required to make future milestone payments for initiation of clinical trials and approval of a New Drug Application ("NDA"). Should ITI commercialize the technology related to this License, ITI would be required to make royalty payments, and would also be required to pay fees under any sublicense agreements with third parties.

In addition, ITI is required to use at least \$1.0 million annually of its resources for the development and commercialization of the technology until ITI submits an NDA. ITI met its spending requirements in 2015. There were no other payments made or required under the License for the years ended December 31, 2015 and 2014.

**7. Commitments and Contingencies**

The Company currently has operating lease agreements with commitments for \$16,255,927 for laboratory and office facilities through 2027.

At December 31, 2015, future minimum lease payments under leases having an initial or remaining non-cancellable lease term in excess of one year are set forth in the table below:

<b>Year</b>	
2016	\$ 0
2017	1,299,845
2018	1,457,008
2019	1,500,718
2020	1,545,740
Thereafter	10,452,616
	<b>\$ 16,255,927</b>

Rent expense for the years ended December 31, 2015, 2014 and 2013 was \$1,385,207, \$853,504 and \$827,479, respectively.

#### **8. Employee Benefit Plan**

The Company sponsors a defined contribution 401(k) plan covering all full-time employees. Participants may elect to contribute their annual pre-tax earnings up to the federally allowed maximum limits. The Company makes a matching contribution of 50% on the first 6% of contributions made by participants. Participant and Company contributions vest immediately. During the years ended December 31, 2015, 2014 and 2013, the Company recorded matching contribution expense of \$109,963, \$84,757 and \$77,138, respectively.

F-21

**Table of Contents****9. Related Parties**

In the first quarter of 2015, the Company moved its headquarters to 430 East 29th Street, New York, New York 10016. The Company has entered into a long-term lease for approximately 16,753 square feet of useable laboratory and office space. The lease has a term of 12 years. Due to the amortization of total lease payments, the Company has recognized \$1.6 million of deferred rent in the 12 months ended December 31, 2015. The deferred rent balance will incrementally increase over the next two years. A member of the Company's board of directors is the Chairman of the board of directors, Chief Executive Officer and President of the parent company to the landlord under this lease.

**10. Unaudited Quarterly Financial Information**

The tables herein set forth the Company's unaudited condensed consolidated 2015 and 2014 quarterly statements of operations.

*The following table sets forth the Company's unaudited condensed consolidated statements of operations for the 2015 quarters ended:*

<b>2015 Quarter Ended</b>	<b>December 31,</b>	<b>September 30,</b>	<b>June 30,</b>	<b>March 31,</b>
Revenue	\$ 30,659	\$	\$ 57,390	\$ 3,315
Net loss	(28,834,516)	(32,160,483)	(21,511,318)	(22,286,824)
Basic and diluted net loss per share	\$ (0.67)	\$ (0.91)	\$ (0.61)	\$ (0.72)

*The following table sets forth the Company's unaudited condensed consolidated statements of operations for the 2014 quarters ended:*

<b>2014 Quarter Ended</b>	<b>December 31,</b>	<b>September 30,</b>	<b>June 30,</b>	<b>March 31,</b>
Revenue	\$ 65,862	\$ 124,414	\$ 219,238	\$ 167,787
Net loss	(15,199,130)	(6,415,507)	(4,533,539)	(4,543,284)
Basic and diluted net loss per share	\$ (0.52)	\$ (0.22)	\$ (0.15)	\$ (0.17)